The International Society of Exercise and Immunology

13th ISEI Symposium

Training our immune system for health and performance

11th–14th July 2017

Faculty of Sport Science & Physical Education, University of Coimbra
Coimbra, Portugal

CÂMARA MUNICIPAL DE COIMBRA

FCT
Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

Santander Totta

HOLMES PLACE

WELCOME

to the 13th Symposium of the International Society of Exercise and Immunology

The Executive Committee of the **13th International Society for Exercise and Immunology Symposium** (ISEI 2017) welcomes you all to the City of Coimbra.

The 2017 symposium will include presentations by international researchers on areas like the genetic influences of exercise on immunity; the impact of exercise on inflammatory and muscle disorders; the influence of diet and metabolism on immunity; the role of exercise in children and aging populations; and the effect of exercise on disease outcome. Being a post Olympic year we will also focus on areas like athletes' immune health and performance in extreme conditions. It will also include a new exciting session on exercise and the gut microbiota: from brain to muscle.

As in the previous ISEI symposia we aim to attract many early career researchers, but also well-known experts to ensure valuable information exchange. The friendly and open nature that characterizes the ISEI symposia has the potential to foster future projects, collaborations and friendships. The oral and poster awards for young investigators is an opportunity for young scientists to have their work recognized by their peers, and to receive a free registration for the next ISEI symposium in 2019.

The proceedings of this symposium will also be published in the *Annals of Research in Sport and Physical Activity,* and we acknowledge the support of FCT (Fundação para a Ciência e Tecnologia).

When coming to Coimbra you will experience the historical heritage of one of the oldest cities of Portugal, with its many cultural and tourist sites, including the University of Coimbra, which has been classified as World Heritage by UNESCO, but also the relaxing atmosphere of its restaurants and bars, where you can enjoy traditional Portuguese dishes and wines.

Enjoy the meeting and your time in Portugal.

Ana Maria Teixeira

Congress President

Katsuhiko Suzuki

ISEI President

Jonathan Peake

ISEI President Elect

XIII ISEI SYMPOSIUM SCIENTIFIC PROGRAMME

"Training our immune system for health and performance"

Tuesday 11th July	
14:00- 17:30	**Registration**
17:30- 19:30	Welcome Reception (Sta Clara –à-Velha Monastery)
Wednesday 12th July	
8:00- 9:00	Day registration and poster mounting
9:00- 9:30	Opening of the Symposium
9:30- 10:30	**Session 1: Presidential Symposium & Honorary Lecture** Chairs: Maree Gleeson (AUS) and Ana Maria Teixeira (PT)
9:30	**Katsuhiko Suzuki (JP):** Cytokine response to exercise and its modulation
10:00	**Romain Meeusen (BE)**: Exercise and the Brain
10:30- 11:00	Tea/Coffee break
11:00- 12:30	**Session 2 –How to Maintain Athletes Health** Chairs: Nicholas West (AUS) and Luís Rama (PT)
11:00	**Maree Gleeson (AUS):** Regulation of Mucosal Immunity and Impact of Exercise
11:30	**David Pyne (AUS)**: Quantitative interpretation of immune test results in athletes
	Oral presentations
12:00	**Naroa Etxebarria (AUS)**: Lost in translation - Getting your research message across
12:15	**Candice Colbey (AUS)**: Immune cell profiles distinguish Australian Olympic athletes with or without URS
12:30- 14:00	Lunch
14:00- 15:30	**Session 3 – Immune Responses to Exercise** Chairs: Neil Walsh (UK) and Cristina Monteiro (PT)
14:00	**Karsten Krüger (GE):** Exercise, lymphocyte life span and adaptation

Oral Presentations

14:30	**Selma van Staveren (NL)**: Multidimensional analysis reveals increasing phenotypic changes in the total neutrophil compartment during 8 consecutive days of endurance exercise.
14:45	**Erik D. Hanson (USA)**: Submaximal aerobic exercise induces mait cell lymphocytosis but does not alter homing and activation markers.
15:00	**Diogo V. Leal (UK)**: Endocrine, immune and inflammatory adaptations in men following exercise induced chronic stress.
15:15	**Johanna K. Ihalainen(FI)**: Inflammation status of healthy untrained young men: initial response to resistance training.
15:30	**A. L. Moura (PT):** Anaphylaxis during physical exercise.
15:45- 16:00	Tea/Coffee break
16:00- 17:30	**Session 4 – Immune Responses to Extreme Challenges** Chairs: Richard Simpson (USA) and Fabian Lim (SG)
16:00	**Neil Walsh (UK) -** Immune Responses to Extreme Challenges

Oral Presentations

16:30	**Austin B. Bingley (USA)**: Dysregulated NK-cell function during long-duration spaceflight.
16:45	**Nadia H Agha(USA)**: The impact of a 6-month mission to the International Space Station (ISS) on salivary antimicrobial proteins.
17:00	**Rhiannon Snipe (AUS)**: Can carbohydrate and protein intake prevent gut-immune perturbations induced by exertional-heat stress?
17:15	**Mauro Vaisberg (BR)**: Differences in the nasal neutrophil count between marathoners with or without exercise-induced bronchoconstrition.
17:30	**Karsten Krüger (DE)** : Effects of therapeutic exercise training on systemic inflammation in smoke-exposed mice.
17:45-18:45	Poster viewing and judging of Early Career Researcher posters

Thursday 13th July	
8:00- 9:00	Day registration and poster mounting
9:00- 10:30	**Session 5 – Exercise and Metabolism** Chairs: David Nieman (USA) and Raul Martins (PT)
9:00	**Amira Klip (CAN)** - Exercise and Metabolism

Oral Presentations

9:30	**Claúdia R. Cavaglieri (BR)**: Associations between metabolic and inflammatory changes in obese middle-age men after 24 weeks of combined training.
9:45	**Liliana Baptista (PT)**: Multifactorial cardiovascular risk intervention in an early stage of Type 2 diabetes in older adults: the effect of exercise training and metformin.
10:00	**Arwel W. Jones (UK)**: Vitamin D status modulates innate immune responses and metabolic profiles following acute prolonged cycling.
10:15	**Melissa M. Markofski (USA)**: Moderate activity, not vigorous activity is associated with a higher percent of circulating classic monocytes positive for CX3CR1 and CCR2.
10:30	**Loreana Silveira (BR)**: Peritoneal macrophage and adipose tissue macrophage polarization in obese mice: role of exercise training and PPAR-γ.
10:45- 11:00	Tea/Coffee break
11:00- 12:30	**Session 6 – Skeletal Muscle Regeneration and Adaptation** Chairs: David Pyne (AUS) and Carlos Fontes Ribeiro (PT)
11:00	**Benedicte Chazaud (FR):** Macrophages during skeletal muscle regeneration: from experimentation in mouse to human physiology
11:30	**Jonathan Peake (AUS):** Profiling Skeletal Muscle Injury and Regeneration Using Proteomics

Oral communications

12:00	**Oliver Neubauer (AUS)**: Novel time-course related linkages of skeletal muscle gene networks with blood inflammation and muscle damage markers following endurance exercise.
12:15	**Yuzuru Sakamoto (JP):** A role of DAP12, an activating-type immunoregulatory molecule in skeletal muscle regeneration
12:30- 14:00	Lunch (ISEI Board Meeting – Sala Jardim)
14:00- 15:30	**Session 7 – Modulating Diseases Outcome by Exercise** Chairs: Karsten Kruger (GE) e Benoit Dugué (FR)
14:00	**Pernille Hojman (DK):** Running from Cancer: A Role for Exercise-Mediated Control of Cancer Through Regulation of Immune Function.
14:30	**Ryoichi Nagatomi (JP):** Lessons from Natural Killer Deficient Patients – Implication In Exercise Immunology

Oral communications

15:00	**Michael Harrison (IR)**: Influence of sprint interval exercise and continuous aerobic exercise on circulating angiogenic leukocytes in older adults.
15:15	**Sven P. Hoekstra (SW)**: Elevated core temperature: not only useful in the context of exercise to combat chronic low-grade inflammation?
15:30	Testimony of a patient with Rheumatoid Arthritis (Sponsored by Holmes Place)
15:45- 16:00	Tea/Coffee break
16:00- 17:30	**Session 8 – Nutritional Intervention in Exercise** Chairs: Claúdia Cavaglieri (BR) and Jonathan Peake (USA)
16:00	**David Nieman (USA):** Impact of Nutrition on Metabolic and Immune System Recovery from Heavy Exertion: Value of Multi-Omics Approaches
16:30	**Lindy Castell (UK):** Can Nutritional Supplements Help Exercise-induced Immunodepression?

Oral communications

17:00	**Glen Davison (UK):** Bovine Colostrum supplementation enhances sensitivity of the in vivo immune response to a novel antigen following prolonged exercise.
17:15	**Matheus Uba-Chupel (PT):** Exercise and supplementation with taurine in the elderly: effects on immune and blood-brain barrier integrity markers.
17:30	**Juliana Santos (BR):** Influence of Vitamin D and inflammation on sleep disorders in sedentary and street runners.
17:45- 18:45	Poster viewing and judging of Earlier Career Researcher Award
19:30	Symposium Dinner – Quinta das Lágrimas

Friday 14th July

9:00- 10:30	**Session 9 – Immunosenescence and Exercise** Chairs: Eduardo Ortega (ES) and Barbara Wessner (AT)
9:00	**Richard Simpson (USA):** Mobilizing T-Cells With Exercise for Adoptive Transfer Immunotherapy
9:30	**Ana Teixeira (PT):** Effects of Lifelong Training on T Lymphocytes Senescence

Oral presentations

10:00	**Forrest L. Baker (USA):** Relationships between cardiorespiratory fitness and markers of senescence and exhaustion in peripheral blood CD8+ T-cells and NK-cells.

10:15	**Masataka Uchida (JP)**: Chronic responses of inflammation and macrophage function to exercise training in various tissues of senescent mice.
10:30- 11:00	Tea/Coffee break
11:00- 12:30	**Session 10 – Exercise and the Gut Microbiota: From Brain to Muscle** Chairs: Ryoichi Nagatomi (JP) and José Pedro Ferreira (PT)
11:00	**Monika Fleshner (USA):** Early Life Exercise Promotes Favorable Changes in Gut Microbial Ecology, Persistent Stress Robustness, and Metabolic Health"
11:30	**Jorge Ruas (SW):** The Effects of Exercise Training on Kynurenines, Metabolism, and Mental Health
	Oral presentations
12:00	**Nicholas West (AUS)**: Exercise, the microbiota and immune regulation.
12:15	**Bernardo A. Petriz (BR):** Analysis of moderate aerobic exercise on the gut microbiota from mice induced to obesity with high fat diet.
12:30- 13:30	Closing of the Symposium and Earlier Career Researcher Awards (Sponsored by iKeys)

Farewell

We would like to thank the European Office for Aerospace Research & Development who kindly contributed to the costs of our conference

Poster Session A (12.07.07)

P01 - MODIFICATIONS IN HAEMATOLOGICAL INDICES OF UNIVERSITY ATHLETES FOLLOWING SOCCER COMPETITION

Moses Monday Omoniyi; Osei Francis; Baffour-Awuah Biggie; Asamoah Benjamin; Appiah Eric Junior; Akwa Lady Gwendoline

P02 - EFFECT OF DIFFERENT LOADS OF TREADMILL EXERCISE ON TH1/TH2 BALANCE OF ISOLATED SPLENOCYTES IN RAT

Zahra Gholamnezhad, Mohammad Hossein Boskabady

P03 - THE EFFECT OF PROLONGED REPEATED MODERATE INTENSITY EXERCISE ON CYTOKINE CONCENTRATIONS IN ADULTS

R. Terink; C.W.G. Bongers; R.F. Witkamp; M. Mensink; J.M.T. Gunnewiek; M.T. Hopman

P04 - COMPARABLE NEUTROPHIL RESPONSES FOR ARM AND INTENSITY-MATCHED LEG EXERCISE

Christof A. Leicht; Victoria L. Goosey-Tolfrey; Nicolette C. Bishop

P05 - EFFECTS OF CAFFEINE SUPPLEMENTATION ON CYTOKINE RESPONSE TO A TREADMILL EXERCISE TEST

Pedro Tauler; Lluis Rodas; Carlos Moreno; Antoni Aguiló; Sonia Martínez

P06 - RELATIONSHIP BETWEEN THE STABILITY AND EMOTIONAL STABILITY OF SPORTS PERFORMANCE AND CHANGES IN GUT MICROBIOTA WITH MENTAL AND PHYSICAL STRESS

Kaori Matsuo; Kazunobu Okazaki; Kazusige Goto; Kenji Takao; Hiroshi Sato; Ryoichi Nagatomi; Hiromi Yano; Shin Fukudo

P07 - CAN INTERVALS ENHANCE THE INFLAMMATORY RESPONSE AND ENJOYMENT IN UPPER-BODY EXERCISE?

Sven P. Hoekstra; Nicolette C. Bishop; Christof A. Leicht

P08 - POTENTIAL OF TEAR FLUID ANTIMICROBIAL PROTEINS TO EVALUATE RISK OF UPPER RESPIRATORY ILLNESS

Helen G. Hanstock; Jason P. Edwards; Neil P. Walsh

P09 - THE EFFECT OF PROFESSIONAL SPORT TRAINING ON CIRCULATING MARKERS OF ASEPTIC VASCULAR INFLAMMATION

Tylutka Anna; Morawin Barbara; Baumgarten Maciej; Kamiński Krzysztof; Pokrywka Andrzej; Zembroń-Łacny Agnieszka

P10 - DOWNHILL EXERCISE INDUCES INCREASE OF INFLAMMATORY CYTOKINES IN TRICEPS BRAQUII OF MICE WITH OPPOSITE RESPONSE BETWEEN IL-4 AND IL-13 AT 72 HOURS AFTER

Andre Luis Araujo Minari; Aline Venticique Caris; Ronaldo Thomatieli dos Santos

P11 - EFFECTS OF CAFFEINE SUPPLEMENTATION ON LPS-INDUCED EX VIVO CYTOKINE PRODUCTION FOLLOWING EXERCISE

Sonia Martínez; Lluis Rodas; Leticia Lozano; Antoni Aguiló; Pedro Tauler

P12 - CHANGES IN INFLAMMATORY MOLECULES FOLLOWING MODERATE INTENSITY CONTINUOUS AND HIGH INTENSITY INTERMITTENT ACUTE EXERCISES IN YOUNG HEALTHY MEN

Daniel Massote Magalhães; Guilherme Carvalho Rocha; Lucas Neves Vaz; Marcelo Henrique Salviano de Faria; Albená Nunes-Silva; Natália Pessoa Rocha; Erica Leandro Marciano Vieira; Ana Cristina Simões e Silva

P13 - PLASMA AND URINE LEVELS OF IRISIN IN RESPONSE TO MODERATE INTENSITY CONTINUOUS AND TO HIGH INTENSITY INTERMITTENT ACUTE EXERCISES

Daniel Massote Magalhães; Lucas Neves Vaz; Guilherme Carvalho Rocha; Erica Leandro Marciano Vieira; Marcelo Henrique Salviano de Faria; Natália Pessoa Rocha; AlbenáNunes-Silva; Ana Cristina Simões e Silva

P14 - THE ROLE OF INFLAMMATION IN PHYSICAL TRAINING INDUCED SKELETAL MUSCLE REMODELING: THE REACTIVE OXYGEN SPECIES (ROS) PARTICIPATION

Luiz Alexandre Medrado de Barcellos; Barbara Maximino Rezende; William Antônio Gonçalves; Walyson Coelho Costa; Cândido Celso Coimbra; Albená Nunes Silva; Vanessa Pinho

P15 - EXERCISE TRAINING-INDUCED CHANGES IN INFLAMMATORY MEDIATORS AND HEAT SHOCK PROTEINS IN CANOEISTS

Morawin Barbara; Tylutka Anna; Baumgarten Maciej; Rynkiewicz Mateusz; Zembroń-Łacny Agnieszka

P16 - ACUTE AND CHRONIC IL-6 RESPONSES DURING FULL SEASON TRAINING IN YOUNG SWIMMERS

D. Nafpaktitou, A. Philippou, G. Vagiakakos, N. Vagiakakos, M. Mantaloufas, G. Chrousos, M. Koutsilieris, and T. Platanou

P17 - EFFECT OF PROBIOTICS SUPPLEMENTATION ON FUNCTION OF MONOCYTES AND URTI AFTER MARATHON

Edgar T Silva; André A Minari; Aline V Caris; Samile A Santos; Graziela R Ravacci; Sergio Tufik; Ronaldo VT Santos

P18 - LIFELONG TRAINING HELPS MAINTAINING CD4 AND CD8 NAÏVE T-CELLS WHILE REDUCING THE NUMBER OF SENESCENT NAÏVE T CELLS

Luciele G Minuzzi; Luis Rama; Fatima Rosado; António Martinho; Artur Paiva; Ana Maria Teixeira

P19 - REACTIVATION OF EPSTEIN-BARR VIRUS FOLLOWING PROLONGED CYCLING

Eleanor Hynes; Glen Davison

P20 - MUCOSAL IMMUNE MARKERS IN PROFESSIONAL ENGLISH FOOTBALL PLAYERS

Eleanor Hynes; Glen Davison

P21 - THE COMPARISON EFFECT OF OVERTRAINING AND OVERTRAINING PLUS VIT D3 ON MIR181B AND INFLAMMATORY FACTORS IN WISTAR RATS

Omid Salehian; Rahman Soori; Ali Asghar Ravasi; Siroos Choobineh

P22 - THE EFFECT OF CRANBERRY ON LEVELS OF INFLAMMATORY AND ANTI-INFLAMMATORY PLASMA CYTOKINES DURING 10-WEEK OF INTENSIVE TREADMILL TRAINING IN ENDURANCE

Omid Salehian; Mohammad Rashidi; Zahra Dadashzadeh

P23 - THE COMPARISON OF ENDURANCE TRAINING WITH MODERATE INTENSITY AND OVERTRAINING ON TH1/TH2 BALANCE IN WISTAR MALE RATS

Omid Salehian; Nader shakeri

P24 - THE COMPARISON EFFECT OF OVERTRAINING AND OVERTRAINING PLUS VIT D3 ON CYTOKINE KINETICS IN WISTAR RATS

Omid Salehian; Mohammad Rashidi; Golbarg Shabani Jafarabadi

P25 - ANTIINFLAMATORY EFFECTS OF EXERCISE TRAINING IN ANIMALS EXPOSED TO DIESEL EXHAUSTED PARTICLES

Clarice Rosa Olivo; Thamyres Barros Pereira de Castro; Alyne Riane; Tuane N Regonha; Luciano Delesposte; Paula Fernandes; Dolores H R F Rivero; Rodolfo de Paula Vieira; Carla Máximo Prado; Beatriz M. Saraiva-Romanholo; Fernanda DTQS Lopes; Milton de Arruda Martins

P26 - EFFECT OF STRENGTH TRAINING SESSION ON IMMUNOLOGICAL AND PHYSIOLOGICAL BLOOD MARKERS

Ayla Karine Fortunato; Washington Martins Pontes; Kelerson Pinto; Daisy Motta; Debora Souza; Ana Menezes; Everton Rocha Soares; Rodrigo Pereira Da Silva; Erica Leandro Marciano Vieira; André Talvani; Albená Nunes-Silva

P27 - CHANGES IN THE IMMUNE RESPONSE DURING AN ATHLETICS TRAINING AND COMPETITION SEASON IN 800 M HIGH-LEVEL ATHLETES

Beatriz Bachero-Mena; Fernando Pareja-Blanco; Juan José González-Badillo

P28 - THE EFFECT OF CHLORELLA PYRENOIDOSA SUPPLEMENTATION ON IMMUNE RESPONSES TO TWO DAYS OF INTENSIFIED TRAINING

Corinna Chidley; Glen Davison

P29 - ACUTE AND CHRONIC SYSTEMIC IRISIN RESPONSES DURING FULL SEASON TRAINING IN YOUNG SWIMMERS

Dimitra Nafpaktitou; Anastassios Philippou

P30 - CYTOKINE PRODUCTION IN LPS-STIMULATED WHOLE BLOOD CULTURES FROM CONTINUOUS EXERCISES PERFORMED AT DIFFERENT INTENSITIES IN WELL-TRAINED MEN

Barbara de Moura Mello Antunes; Eduardo Zapaterra Campos; Sérgio Souza Parmezzani; Fábio Santos Lira

P31 - EFFECT OF STRENGTH TRAINING SESSION ON IMMUNOLOGICAL AND PHYSIOLOGICAL BLOOD MARKERS

Ayla Karine Fortunato; Washington Martins Pontes; Kelerson Pinto; Daisy Motta; Debora Souza; Ana. P. J Menezes; Everton Rocha Soares; Rodrigo Pereira Da Silva; Erica Leandro Marciano Vieira; André Talvani; Albená Nunes-Silva

P32 - IMMUNE AND HEMATOLOGICAL CHARACTERISTICS OF 2016 OLYMPIC CHAMPION SHOOTING ATHLETE: A CASE STUDY INVESTIGATION IN TRANSITION PERIOD TRAINING

Vu Viet Bao; Le Quy Phuong

P33 - INFLAMMATION PREDICTS PERFORMANCE IN MARATHONERS WITH EXERCISE-INDUCED BRONCHOCONSTRICTION

Juliana de Melo Batista dos Santos; Luiz Antonio Luna Junior; Roberta Foster; André Luis Lacerda Bachi; Ana Paula Rennó Sierra; Marino Benetti; Nabil Ghorayeb; Maria Augusta Dall Mollin Kiss; Rodolfo de Paula Vieira; Mauro Vaisberg

P34 - EFFECTS OF ORAL GLUTAMINE SUPPLEMENTATION ON PLASMA LYMPHOCYTES COUNT AFTER EXHAUSTIVE RESISTANCE EXERCISE

Panayiotou George; Smilios Ilias; Douda Hele; Tokmamidis Savvas; Panayiotou G.; Smilios, I.; Douda, H and Tokmakidis, S.

P35 - MOOD STATES AND CYTOKINE CORRELATION IN FEMALE SOCCER PLAYERS WITH AND WITHOUT PREMENSTRUAL SYNDROME (PMS)

Roberta Foster; Mauro Vaisberg; Juliana de Melo Batista dos Santos; Luiz Antonio Luna Junior; André Luis Lacerda Bachi; Marcia Aparecida Martins; Rodolfo de Paula Vieira; Maíta Poli Araújo; Tatiana Rebizzi Parmigiano; Zsuzsanna Ilona Katalin de Jármy Di-Bella

P36 - EXPERIMENTAL IMMUNOSTRENGTHENING PRACTICES OF HIGH PERFORMANCE SPORT: HOLISTIC FITNESS APPROACH

Peter Smolianov; Jed Smith; Steven Dion; Christopher Schoen; Jinghang Cui

P37 - TRAINING INFLUENCES THE ACUTE IMMUNE RESPONSE TO A MAXIMAL SWIMMING TEST

Cristina Paula Monteiro; José Pedro Morgado; Catarina Nunes Matias; Joana Filipa Reis; Maria José Laires; Francisco Alves

P38 - ANXIETY AND PERCEIVED PSYCHOLOGICAL STRESS PLAY AN IMPORTANT ROLE IN THE IMMUNE RESPONSE AFTER EXERCISE

Jason P. Edwards; Neil P. Walsh; Bethany C. Diment; Ross Roberts

P39 - INFLUENCE OF A-ACTININ-3 (ACTN3) ON INFLAMMATORY MARKERS AFTER ENDURANCE EXERCISE

Maria F. Cury-Boaventura; Ana P. R. Sierra; Rodrigo A. Oliveira; Elton D. Silva; Giscard H. O. Lima; Marino P. Benetti; Maria A. Kiss; Carlos A. Sierra; Nabil Ghorayeb; João B. Pesquero

Poster Session B (13/07/07)

P40 - CYTOTOXIC ACTIVITY OF NN-32 TOXIN FROM INDIAN SPECTACLED COBRA VENOM ON HUMAN BREAST CANCER CELL LINE

Saurabh Attarde; Sangeeta Pandit

P41 - EFFECT OF MODERATE PHYSICAL EXERCISE ON LEUKOCYTE PROFILE IN TUMOR MICROENVIRONMENT AND MELANOMA GROWTH IN MICE ON A HIGH-FAT DIET

Cesar Miguel Momesso dos Santos; Vinícius Leonardo Diniz; Andre Luis Lacerda Bachi; Laiane Cristina dos Santos; Tamara Gazhal; Maria Elizabeth Pereira Passos; Heloisa Helena de Oliveira; Gilson Murata; Laureane N. Mazi; Amanda R Martins; Adriana C. Levada-Pires; Rui Curi[1]; Sandro Massao-Hirabara; Tania C. Pithon-Curi; Renata Gorjão

P42 - EFFECTS OF EXERCISE TRAINING ON PROSTATE DIMENSIONS IN A RAT MODEL OF PROSTATE CANCER

Ana Isabel Faustino; Miguel Correia-Cardoso; Magda SS Moutinho; Milene Rodrigues Ribeiro; Carolina N Fonseca; Rita Ferreira; Margarida Fardilha; Paula A. Oliveira; Mário Ginja

P43 - RESISTANCE TRAINING REDUCES T HELPER CYTOKINE LEVELS BUT NOT CARDIOMETABOLIC RISK FACTORS IN HIV-INFECTED INDIVIDUALS RECEIVING ART

Takshita Sookan; Jose Antonio; Michael J. Ormsbee; Nombulelo P. Magula; Ayesha A. Motala; Umesh G. Lalloo; Andrew J. McKune

P44 - ADIPOKINES LEVELS IN RESPONSE TODIFFERENT INTENSITY PHYSICAL EXERCISE PROTOCOLS IN YOUNG HEALTHY MEN

Daniel Massote Magalhães; Lucas Neves Vaz; Guilherme Carvalho Rocha; Natália Pessoa Rocha; Marcelo Henrique Salviano de Faria; Erica Leandro Marciano Vieira; AlbenáNunes-Silva; Ana Cristina Simões e Silva

P45 - EXHAUSTING EXERCISE IN YOUNG RATS: EFFECT ON SYSTEMIC AND INTESTINAL LYMPHOID TISSUES

Estruel-Amades, Sheila; Massot-Cladera, Malen; Camps-Bossacoma, Mariona; Garcia-Cerdà, Pau; Franch, Àngels; Pérez-Cano, Francisco J.; Castell, Margarida

P46 - PHYSICAL EXERCISE WITH DIFFERENT INTENSITIES ACUTELY MODULATES BOTH AXES OF THE RENIN-ANGIOTENSIN SYSTEM IN HEALTHY SUBJECTS

Daniel Massote Magalhães; Guilherme Carvalho Rocha; Lucas Neves Vaz; Albená Nunes-Silva; Marcelo Henrique Salviano de Faria; Erica Leandro Marciano Vieira; Natália Pessoa Rocha; Ana Cristina Simões e Silva

P47 - FATIGUING EXERCISE ALTERS LEUKOCYTE SUBPOPULATION FREQUENCY IN THE BONE MARROW AND PERIPHERAL BLOOD IN C57BL/6 MICE

Daniela Silva De Oliveira; Laís Roquete Lopes; Débora Maria Soares De Souza; Barbara Maximino Rezende; Vanessa Pinho Da Silva; André Talvani; Albená Nunes-Silva

P48 - EFFECTS OF ACUTE EXHAUSTIVE EXERCISE ON MONOCYTE SUBSETS AND EPIGENETIC MARKERS IN PERIPHERAL MONONUCLEAR CELLS OF LEAN AND OBESE MALES

Gilson Dorneles; Maria Carolina R Boeira; Lucas L Schipper; Ivy RV Silva; Viviane R Elsner; Alessandra Peres; Pedro RT Romão

P49 - CARDIORESPIRATORY FITNESS MODULATES THE ACUTE RESPONSE OF MEMORY TREG AND MEMORY EFFECTOR OF T CELLS TO INTERVAL EXERCISE IN OBESE MEN

Gilson Dorneles; Lucas L Schipper; Maria Carolina R Boeira; Alessandra Peres; Pedro RT Romão

P50 - EXERCISE IS MORE EFFECTIVE THAN METFORMIN TO IMPROVE HEALTH RELATED QUALITY OF LIFE AND MOOD STATES IN OLDER ADULTS WITH TYPE 2 DIABETES

Liliana Carina Pereira Baptista; Raúl A. Martins

P51 - THE EFFECT OF ANTIHYPERTENSIVE MEDICATION AND EXERCISE TRAINING ON FUNCTIONAL STATUS IN HYPERTENSIVE OLDER ADULTS

Liliana Carina Pereira Baptista; Raúl A. Martins

P52 - INCREASED SKELETAL MUSCLE IL-15Rα IS ASSOCIATED WITH MYOFIBRILLAR PROTEIN SYNTHESIS IN RESPONSE TO A SINGLE SESSION OF RESISTANCE EXERCISE

Alberto Pérez-López; James McKendry; Marcos Martin-Rincon; David Morales-Alamo; Barbara Pérez-Köhler; David Valadés; Julia Buján; José A.L. Calbet; Leigh Breen

P53 - WHAT IS THE EFFECT OF A FAST FOOD VERSUS A MEDITERRANEAN MEAL IN THE ADIPOKINE RESPONSE TO AN EXERCISE CHALLENGE?

Diana Silva; Rita Moreira; Marília Beltrão; Oksana Sokhatska; Tiago Montanha; Andreia Pizarro; Mariana Pinto; Vanessa Garcia-Larsen; Rodrigo Villegas; Luís Delgado; Pedro Moreira; Joana Carvalho; André Moreira

P54 - INFLAMMATORY BIOMARKERS AND OXIDATIVE STRESS ENZYMES IN YOUNG WOMEN UNDERGOING MUSCULAR HYPERTROPHY TRAINING

Kelerson Mauro de Castro Pinto; Mauro Heleno Chagas; Rodrigo Cesar Ribeiro Diniz; Grazielle dos Santos Figueria; Karine Beatriz Costa; Guilherme de Paula Costa; Albena Nunes da Silva; Eduardo Bearzoti; Etel Rocha Vieira; André Talvani

P55 - NO EFFECT OF ACUTE OR CHRONIC BOVINE COLOSTRUM SUPPLEMENTATION ON CIRCULATING INSULIN-LIKE GROWTH FACTOR-

Arwel W Jones; Glen Davison

P56 - THE INFLUENCE OF USING DIFFERENT SOUNDS CHICKEN ON IMMUNOLOGICAL AND PHYSIOLOGICAL TRAITS OF BROILER

Salwan Abdulateef; Ziyad Aldhanki; Saman Rashid

P57 - BASELINE NATURAL KILLER CELL CYTOTOXICITY IS ENHANCED IN THE PRESENCE OF POST-EXERCISE AUTOLOGOUS SERUM

Priti Gupta; Austin Bigley; Emily C. LaVoy

P58 - ELDERLY PEOPLE PRACTITIONERS OF A COMBINED EXERCISE TRAINING SHOWS IMPROVEMENT OF SPECIFIC ANTIBODIES IN RESPONSE TO INFLUENZA VIRUS VACCINATION

André L.L. Bachi; Luiz R. Ramos; Daniela S. Rosa; Lika Osugui; Mauro Vaisberg; Jose D. Lopes

P59 - PPAR-γ ACTIVATION RESTORES LIVER INFLAMMATION AFTER CHRONIC EXERCISE IN PPAR-α KNOCKOUT OBESE MICE.

Helena Angelica Pereira Batatinha; Alexandre Abilio Teixeira; Camila Oliveira Souza; Edson Lima; Luana Biondo; Loreana Sanches; Fabio Santos Lira; Jose Cesar Rosa Neto

P60 - EFFECT OF LACTIC ACID BACTERIA ON MUCOSAL IMMUNOLOGY AGAINST E.COLI INFECTION IN POULTRY BIRDS

M. Abubakar Siddique

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ORAL PRESENTATIONS ABSTRACTS

13th Symposium of the International Society of Exercise and Immunology

CYTOKINE RESPONSE TO EXERCISE AND ITS MODULATION

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Key words: systemic inflammation, heat stress, energy and fluid supply.

Exhaustive endurance exercise has been shown consistently to induce leukocytosis due to neutrophilia (systemic inflammation), muscle and organ damage and immune suppression (1-5). To determine the underlying mechanisms of these phenomena, much attention has been focused on cytokines released into the circulation following exercise, and indeed there has been a tremendous accumulation of research findings. Many studies have consistently shown that IL-6, IL-8, IL-1 receptor antagonist (IL-1ra) and IL-10 increased remarkably following endurance exercise longer than 2 h, such as marathon and triathlon (2-5,10,15,18,20), but the response of these cytokines is not so significant during short-duration intensive exercise and eccentric exercise (7,9,14,19,32). These responses are not dependent on exercise-induced muscle damage (inflammation), but are related to exercise intensity (physiological load/stress) (6-8). Indeed, it has been demonstrated that IL-6 response to exercise depends on energy crisis and heat stress, and are correlated with stress hormone responses, but are suppressed by increased energy supply and prior body-cooling interventions (12,13,16,21,22). IL-6 also enhances recruitment of energy substrates, such as free fatty acids, which contributes to endurance performance (5,26). At the same time, IL-6 induces neutrophil mobilization and activation together with immunosuppressive cytokine release of IL-1ra and IL-10 (1-3). Therefore, IL-6 might be good for athletes in optimizing fuel utilization for endurance performance on one hand, but may compromise the immune status of the athlete on the other hand in terms of systemic inflammation and increased susceptibility to infections. It is possible that appropriate countermeasures such as exercising in cool environments, and ensuring sufficient energy and fluid supply together with some functional food might help to maintain endurance performance without causing the harmful side effects on health (11,17,20-23,28). These countermeasures may lead to the introduction of new research findings.

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EXERCISE AND THE BRAIN

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Key words: Neurotransmission, neurogenesis, polyphenols

Introduction

Physical activity has been associated with the reduction of a number of physical and mental disorders. There is now ample evidence that physical activity decreases the incidence of cardiovascular disease, colon and breast cancer, and obesity, but also diseases such as Alzheimer's disease (AD), depression, and anxiety.

Neuroinflammation is a defense mechanism aimed at protecting the central nervous system (CNS) against infectious insults and injury. In most cases, it constitutes a beneficial process that ceases once the threat has been eliminated and homeostasis has been restored3. However, long duration neuroinflammatory processes may lead to a progressive neuronal damage observed in many neurodegenerative disorders, most notably Parkinson's disease (PD) and AD, and also with neuronal injury associated with stroke7.

Nutrition has classically been perceived as a means to provide energy and building materials to the body. However, its ability to prevent and protect against diseases is starting to be recognized. Nutrition and exercise are therefore used as interventions to reverse these possible negative health effects.

Exercise and neurogenesis

Animal research has shown that enriched environments, including access to running wheels, has a positive effect on neuronal growth and on the neural systems that are involved in learning and memory. This neuroplasticity refers to the ability of the brain to adapt to environmental change, respond to injury, and to acquire novel information by modifying neural connectivity and function. Neurotrophins support neuroplasticity, and they are capable of signaling neurons to survive, differentiate, or grow. Neurotrophic factors not only play a role in neurobiology, but also in central and peripheral energy metabolism4. Their effect on synaptic plasticity in the CNS involves

elements of cellular energy metabolism. Acute exercise and training seem to be key interventions to trigger the processes through which neurotrophins mediate energy metabolism and neural plasticity. Of all neurotrophins, brain-derived neurotrophic factor (BDNF) seems to be the most susceptible to regulation by exercise and physical activity4. BDNF has a wide repertoire of neurotrophic and neuroprotective properties in the CNS and the periphery. These include neuronal protection and survival, neurite expression, axonal and dendritic growth and remodeling, neuronal differentiation, and synaptic plasticity such as synaptogenesis in arborizing axon terminals, and synaptic transmission efficacy.

In the search of mechanisms underlying plasticity and brain health, exercise is known to induce a cascade of molecular and cellular processes that support (brain) plasticity. BDNF could play a crucial role in these mechanisms.

Nutrition and the Brain

There has recently been growing interest, supported by a number of epidemiological and experimental studies, on the possible beneficial effects of polyphenols on brain health5. Polyphenols are abundant micronutrients in plant-derived foods and are powerful antioxidants. Fruits and beverages such as tea, red wine, cocoa, and coffee are major dietary sources of polyphenols. Polyphenols have been reported to exert their neuroprotective actions through the potential to protect neurons against injury induced by neurotoxins, an ability to suppress neuroinflammation, and the potential to promote memory, learning, and cognitive function6. Despite significant advances in understanding the biology of polyphenols, they are still mistakenly regarded as simply acting as antioxidants. However, recent evidence suggests that their beneficial effects involve decreases in oxidative/inflammatory stress signaling, increases in protective signaling and neurohormetic effects, leading to the expression of genes that encode antioxidant enzymes, neurotrophic factors, and cytoprotective proteins8. This potential may reside in a number of physiological functions, including their antioxidant properties, their interactions with intracellular signaling pathways, the regulation of cell survival/apoptotic genes and mitochondrial function7.

The largest group of polyphenols is the flavonoids. There are six dietary groups of flavonoids: flavones (e.g. apigenin, luteolin), which are found in parsley and celery; flavanones/flavanonols (e.g. hesperetin, naringenin/astilbin, engeletin), which are

mainly found in citrus fruit, herbs (oregano), and wine; isoflavones (e.g. daidzein, genistein), which are mainly found in soy and soy products; flavonols (e.g. kaempferol, quercetin), which are found in onions, leeks, and broccoli; flavanols [e.g. (?)-catechin, (-)-epicatechin, epigallocatechin, and epigallocatechin gallate], which are abundant in green tea, red wine, and chocolate; anthocyanidins (e.g. pelargonidin, cyanidin, andmalvidin), whose sources include red wine and berry fruits. The nonflavonoid group of polyphenols may be separated into two different classes: the phenolic acids, including the hydroxybenzoic acids (C1–C3 skeleton) and hydroxycinnamic acids (C3–C6 skeleton), and the stilbenes (C6–C2–C6 skeleton). Caffeic acid is generally the most abundant phenolic acid, and is mainly found as the quinic ester, chlorogenic acid, in blueberries, kiwis, plums, and apples. Resveratrol, the main stilbene, can be found in the cis or trans configurations, either glucosylated (piceid) or in lower concentrations as the parent molecule of a family of polymers such as viniferins, pallidol, or ampelopsin A. Resveratrol dietary sources include grapes, wine, and peanuts5.

Polyphenols have been associated with a reduced risk of developing dementia, an improved cognitive performance in normal aging and an improved cognitive evolution. The neuroprotective actions of dietary polyphenols involve a number of effects within the brain, including a potential to protect neurons against injury induced by neurotoxins, an ability to suppress neuroinflammation, and the potential to promote memory, learning, and cognitive function. While many of the mechanisms underpinning their beneficial effects remain to be elucidated, it has become clear that they partly involve decreases in oxidative/inflammatory stress signaling, increases in protective signaling, and may also involve hormetic effects to protect neurons against oxidative and inflammatory stressors. Emerging evidence suggests that dietary-derived flavonoids have the potential to improve human memory and neurocognitive performance by their ability to protect vulnerable neurons, enhance existing neuronal function, and stimulate neuronal regeneration.

Pollution, exercise and nutrition

Today, air pollution is a growing environmental problem worldwide and the high traffic density in urban environments and cities is a major cause of this problem. Air pollution worldwide has been associated with cardiovascular and respiratory

morbidity and mortality, particularly in urban settings with elevated concentrations of primary pollutants. Air pollution is a very complex mixture of primary and secondary gases and particles, and its potential to cause harm can depend on multiple factors—including physical and chemical characteristics of pollutants, which varies with fine-scale location (e.g., by proximity to local emission sources)—as well as local meteorology, topography, and population susceptibility. Recently, air pollution exposure has been linked to adverse effects on the brain such as cognitive decline, neuroinflammation and neuropathology2. Inflammation is considered one of the common and basic mechanisms through which air pollution exposure induces negative health effects1. It is envisioned that the latter effects may be aggravated when doing physical activity outdoor in an urban environment. Ventilation rate increases during exercise and in polluted environments, which results in a substantial enhancement of air pollution inhalation2. The question can be raised whether known benefits of regular physical activity on the brain also apply when physical activity is performed in polluted air. It has been hypothesized that the intake of anti-oxidant and anti-inflammatory nutrients may ameliorate various respiratory and cardiovascular effects of air pollution through reductions in oxidative stress and inflammation. To date, several studies have suggested that some harmful effects of air pollution may be modified by intake of essential micronutrients (such as B vitamins, and vitamins C, D, and E) and long-chain polyunsaturated fatty acids.

The ability of dietary antioxidants to enhance the activity of antioxidant enzymes is vital, as these endogenous enzymes play an integral role in neutralizing the harmful effects of free radicals, such hydrogen peroxide and the superoxide radical. Thus, antioxidant supplementation may be helpful in reducing air pollution-induced oxidative stress in the body, by both direct and indirect mechanisms. Also, cocoa flavanols (epicathechin) may be neuroprotective recent findings suggest that cocoa interventions may be critical for early implementation of neuroprotection of highly exposed urban children. Multi-domain nutraceutical interventions could limit the risk for endothelial dysfunction, cerebral hypoperfusion, neuroinflammation, cognitive deficits, structural volumetric detrimental brain effects, and the early development of the neuropathological hallmarks of Alzheimer’s and Parkinson’s diseases1.

Conclusion

Exercise is a very powerful mean to interact with the brain. It is clear that exercise has a neuroprotective effect and creates neurogenesis. However, exercising in an polluted environment can have negative effects, while some nutritional interventions such as polyphenols can help to protect the brain against negative effects of pollution.

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REGULATION OF MUCOSAL IMMUNUTY AND IMPACT OF EXERCISE

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Key words: mucosal immunity, exercise, salivary IgA, infections, inflammation, microbiome

The first research on the impact of exercise on mucosal immunity was published by Tomasi *et.al* [1] thirty five years ago on the changes in salivary IgA concentrations before and after strenuous exercise in high-performance athletes. There have been many investigations since on the impact of exercise on salivary IgA in different populations, spaning elite to sedentary, young and old, obese and healthy weight, differences in responses between males and females, and across many sports [2, 3]. Much of this research has focused on the role of mucosal immunity in prevention of mucosal infections and use of salivary IgA as a marker to predict athletes at higher risk of upper respiratory illness (URI) [3], or in some situations as a marker for acute and chronic stress responses [4]. Depending on the populations being studied the utilisation of salivary IgA as a predictor of risk of infections has been variable. However, the consensus is that clinically low levels of salivary IgA place a person at increased risk of respiratory infections [3], and changes in S-IgA in response to psychological stress are consistent with increases in response to acute stress, and a decrease over time in response to chronic stressors [4].

While recognising the importance of effective mucosal immunity as the first-line-of-defence against infections, there has been very little research on the impact of exercise on regulation of the mucosal immune system in humans. Research on immune regulation with exercise has been predominantly confined to animal models, mainly due to the difficulty and ethics of undertaking similar investigations in humans. The transferability of animal research to humans is not always perfect and needs to be considered with caution before being implemented as ‘dogma’ for advice to exercising humans.

Regulation of Human Mucosal Immunity

The following summary relies heavily on the consensus information published in the latest edition of *Mucosal Immunology* [5].

Control of mucosal immunity

Effective mucosal immunity relies on the uptake, processing and presentation of antigens that discriminates between harmless antigens and dangerous pathogens or their toxins [6]. A primary role is the production of humoral and cellular factors of innate and specific immunity that prevents overstimulation of the immune system and disruption of the mucosal membrane integrity. The mucosal immune system interacts in a continuous bidirectional manner with the microbiota to ensure an appropriate response that is tightly controlled by anti-inflammatory mechanisms.

The integrity of the epithelial cells lining mucosal surfaces is critical to effective immunity. The tight intercellular junctions, mucociliary actions, physiochemical barriers, and microbial pattern recognition receptors on the epithelia, are all important functions and critical for health. The epithelium is a source of innate humoral factors in the human intestinal and respiratory tracts. While initially pro-inflammatory to attract and activate myeloid and lymphoid cells, the rapid switch to immunosuppressive cytokines (Il-10, TGF-B) and chemokines is necessary to minimise tissue damage. The epithelium plays a key role in non-inflammatory antigen disposal via the polymeric-IgA (pIgA) interacting with the polymeric immunoglobulin receptor (pIgR) on epithelial surfaces.

Dendritic cells (DCs) in the lamina propria or protruding into the lumen between epithelial cells influence the recruitment and differentiation of lymphoid cells. Migration of DCs to the regional lymph nodes induces mucosal T-helper cell (Th17) responses that produce cytokines (IL-17 and IL-22) upregulating S-IgA production, epithelial cell production of antimicrobial proteins and peptides, and pIgR expression. The majority of mucosal T-cells (CD4 and CD8) display phenotypes that are important in rapid cytotoxic responses to infections, particularly virally infected epithelial cells.

Regulation of mucosal defence, immune tolerance to non-pathogenic antigens and maintenance of epithelial barrier integrity by non-inflammatory mechanisms involves intricate interactions between mucosal cellular populations to maintain homeostasis. In addition to innate mucosal lymphoid cells, the T-regulatory cells, produced in the gut-associated lymphoid tissues (GALT) and mesenteric lymph nodes play key roles in controlling inflammation and ensuring epithelial cell growth and repair.

Transfer of immunity via CMIS

Immune responses can be induced locally at all mucosal surfaces in response to local antigen presentation. An important feature of the integrated common mucosal immune system (CMIS) is the ability to confer protective immunity at distant mucosal sites by the transfer of cells from inductive sites, particularly the respiratory and intestinal tracts [6]. The transfer of T-cells from inductive sites provides rapid effector mechanisms at distant mucosal sites, and in addition to protective antibodies in human milk, passive protection of newborns.

As much of the research on the impact of exercise on mucosal immunity has focused on the respiratory tract it is worth commenting on the nasal and bronchial immune systems. The structure of lymphoid tissues in the nasal and oral cavities, and respiratory tract differs between humans and rodents [7]. Unlike rodents, nasal-associated lymphoid tissue (NALT) and bronchus-associated lymphoid tissues (BALT) are not present in every individual and the clusters have a random distribution that is only evident following infection or inflammation. Human NALT and BALT can promote IgA-producing B-cells in response to infections but also prime IgG-producing B-cells in the nasal passage and lung. In response to inhaled allergens NALT and BALT can induce IgE-producing B-cell responses. The dendritic cell and T-cell responses to antigen in NALT and BALT and respiratory tract induce strong cytotoxic T-cell responses that have long-lived memory, and are critical for killing virus-infected epithelial cells. Rapid control of viral reactivation is important particularly in respiratory lymphoid cells with latent viruses such as Epstein Barr Virus (EBV).

Influencing factors

The major factors influencing mucosal immune responses are commensal bacteria and pathogen exposure. The ability to maintain mucosal homeostasis and health are influenced by the following key factors in humans:

- *Genetic inheritance* can influence the regulation of the immune response or tissue repair necessary to avoid inappropriate or uncontrolled inflammatory responses.

- *The microbiome* is impacted by nutrition, probiotic and antibiotic treatments not only in the gastrointestinal tract but at other mucosal sites leading to altered immune responses.
- *Nutritional deficits* of important macro- and micro-nutrients can lead to impaired immune responses.
- *Mucosal infections and allergens* can alter immune responses that result in chronic inflammatory responses or disturbed mucosal epithelial barrier functions, despite appropriate therapeutic interventions
- *Neuronal regulation and stress responses* are critical to effective immune response at mucosal sites [8] not only to infections but other psychological and environmental stressors [4]. The bidirectional interactions between the nervous and immune systems, and the modulating effects of commensal bacteria, regulate the 'gut-brain' communication mechanisms controlling inflammatory responses and epithelial barrier functions.

Impact of Exercise on Human Mucosal Immunity

The impact of exercise on the regulation of the mucosal immune system in humans is not well studied. The limited information available is often inferred from indirect measures or animal studies.

Genetic influences and cytokine responses

Ethnicity impacts on the genetic inheritance of cytokine regulation [9]. Differences in cytokine gene polymorphisms and responses to exercise suggest a genetic predisposition to pro-inflammatory responses in athletes who are prone to URI, and who have impaired regulation of cytokine responses to exercise [10].

A defect in IFN-ɣ secretion [11] has also been associated with athletes experiencing recurrent URI and fatigue, consistent with differences observed in IFN-ɣ genotypes [12].

Mucosal antibodies

The impact of exercise on salivary IgA responses is the most extensively studied field of mucosal immunity [2, 3, 10] but the impact on the regulation of S-IgA has not been

directly investigated. The consensus indicates that changes in salivary IgA concentrations vary with the intensity of exercise, and sustained reductions are predominantly seen in high-intensity endurance training. As in the general population, low levels of salivary IgA are associated with an increased risk of URI in high-performance endurance athletes [2, 3]. Moderate exercise can increase salivary IgA levels and training modifications incorporating this impact can be effective in reducing the incidence of URI [13].

S-IgA concentrations in tear fluid can be predictive of URI in athletes [14]. Gut immunity has predominantly been studied in healthy exercising populations in relation to nutritional and probiotic interventions (discussed below) or disruption of epithelial barriers during intense exercise [15]. Long duration strenuous exercise in the heat can cause increased intestinal permeability and disruption of pathogen responses in humans [16].

Vaccination responses

The impact of exercise on mucosal vaccine responses, as opposed to systemic vaccinations, indicates high performance athletes are capable of mounting appropriate responses [17]. The timing of the vaccination in relation to exercise can boost the response [18].

Nutrition and probiotics

The impact of macro- and micro-nutrients on immunity has recently been reviewed in exercising populations [19] and a balance of all key nutrients is required for effective mucosal immunity. There are no studies on immune regulation at mucosal surfaces in humans.

Similarly, probiotic interventions [19] have focused on maintaining a ‘healthy’ profile of microbiota at gastrointestinal surfaces based on the assumptions of animal studies and interactions between the commensal bacteria, mucosal immune responses and the integrity of epithelial barriers [20]. While human studies are limited, exercise *per se* and interactions with dietary intake can alter the diversity of gastrointestinal microbiota but little is known of the impact on mucosal immune regulation [20].

Innate immune factors

Lactoferrin and lysozyme concentrations in saliva have been incorporated into human studies and provide insight on the acute response to exercise [2, 15]. Recently the response of midkine, an endothelial biomarker, indicated a rapid response to intense exercise that resolves rapidly with cessation of exercise [10], suggesting intense exercise induces an acute 'stress' response. The impact of these innate biomarker responses on regulation of specific mucosal immunity is not clear.

Neuronal interactions and stress responses

Exercise can be a stimulant of a physiological stress response resulting in both positive effects on immune function associated with short term stress responses, and negative effects from prolonged intense exercise, particularly under adverse environmental conditions [18]. The impact on mucosal immune function can only be inferred from measures of neuronal responses to exercise, and their interaction with the immune system and mucosal epithelial integrity.

Conclusion

The impact of exercise on regulation of mucosal immune responses in humans is not well understood and studies are difficult to design. Inference from indirect measures and clinical outcomes are currently the only available outcome measures. Animal-based studies require cautious application to humans.

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QUANTITATIVE INTERPRETATION OF IMMUNE TEST RESULTS IN ATHLETES

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Key words: illness, athlete, statistics, reference range, variability

Effective use of immune system profiling or monitoring in athletes requires a carefully designed and implemented program. A program to improve athlete health typically comprises clinical support, education of athletes, coaches and officials, training management, dietary practices, and occasionally biomedical or immune testing. From a quantitative perspective, the primary issues in interpreting an immune test with confidence include references ranges, the smallest worthwhile change or difference, and various statistical terms. In relation to likely clinical outcomes, clinicians and researchers also need basic knowledge on interpreting odds ratios, risk ratios and hazard ratios. In a research setting there are choices of various analytical approaches from traditional statistical significance, to Bayesian analysis, and other hybrid approaches.

Reference Ranges

A long-standing issue with clinicians and researchers is the availability of sports-specific reference range intervals for haematological, biochemical and immunological measures in athletic populations. The extent to which sports-specific ranges vary in comparison with standard clinical reference values, is unclear. Prospective longitudinal studies are needed to develop sports-specific reference ranges for clinicians in diagnostic and screening settings, and assist researchers clarify the effects of various training, lifestyle, and dietary interventions, and changes in inflammatory control processes. Encouragingly, some preliminary work has been useful in identifying differences in cell counts and markers between sports [1].

Smallest Worthwhile Change or Difference

When interpreting changes in an athlete's immune profile it is important to determine the magnitude of the smallest clinically important change in the immune parameter(s)

of interest, and the likely uncertainty or noise in the test result. Where no direct relationship between the risk of illness and biomarker concentration has been established, an appropriate default approach is one-fifth of the between-subject standard deviation (a standardised or Cohen effect size of 0.20). Uncertainty or noise in a test result is best expressed as the typical or standard error of measurement derived from a reliability study. The noise in quantifying many cellular and soluble immune parameters is often greater than the smallest worthwhile difference, so assessment of changes in the risk of illness can be problematic. Unrealistically large changes can be partially discounted when tests are noisy.

Statistical Terms

In the context of sports medicine, test sensitivity can be defined as the ability of a test to correctly identify those with illness or infection (true positive rate), whereas test specificity refers to the ability of the test to correctly identify those without illness (true negative rate). Interpreting the variability in immunological markers within and between athlete cohorts can be informative. For example, the variability and fluctuation of salivary immunoglobulin concentrations can be consistently greater in elite swimmers, but multiple samples from individual swimmers were less correlated compared with participants with lower physical activity levels [2]. These outcomes have implications for monitoring mucosal immune status within individuals, and when comparing salivary immunoglobulin concentrations between groups with differing levels of physical fitness and activity.

Odds, Risk and Hazard Ratios

The risk ratio (or relative risk) is the ratio of the risk of illness in two groups (for example a group of athletes presenting with illness and a second group of healthy counterparts), whereas the odds ratio is the ratio of the odds of an event. For both measures, a value of 1 indicates that the estimated effects are the same for both interventions (groups). The hazard ratio is defined as the ratio of the hazard rates corresponding to the conditions described by two levels of an explanatory variable. For example, in an athlete study of training loads and illness, an over-trained group may experience upper respiratory illness at twice the rate per unit time as the control group. The hazard ratio would be 2, indicating higher hazard of illness from overtraining. Or in another study, female athletes undertaking the same training may

suffer from illness three times more frequently per unit time than men, giving a hazard ratio of 3. Hazard ratios differ from relative risks and odds ratios in that the latter two are cumulative over an entire study, using a defined endpoint, while hazard ratios represent instantaneous risk over the study time period.

Various measures of illness incidence in athletes include illness risk (proportion of athletes with illness in a given period of training or competition), illness rate (number of illnesses per unit of training), odds of illness (probability that illness will occur divided by probability that illness will not happen), and mean time or mean number of sessions or games to illness. Effects of risk factors are estimated as values of effect statistics representing differences or ratios of one or more of these measures between groups defined by the risk factor. Values of selected ratios and their sampling uncertainty (confidence limits) are estimated with specialised procedures: odds ratios with logistic regression, rate ratios with Poisson regression, and hazard ratios with proportional hazards (Cox) regression [3]. Illness risks and mean time to illness in different groups can also be estimated and often give a better sense of the effect of a risk factor.

Statistical Approaches in Research Studies

The choice of analytical approach for research has generated lots of academic debate. While most clinicians and researchers are taught the basics of statistical significance at university, limitations of significance or hypothesis testing have been well documented [4]. Researchers should have a basic understanding of the shortcoming and misuses of significance testing and improper handling of p-values. Appropriate interpretation of study results should include estimates of magnitudes and precision of estimation (confidence limits). In some ways this choice can be simplified down to frequentist versus Bayesian analysis, although in sports science there has been much debate about the emergence of other non-Bayesian or magnitude-based inference approaches [5]. The merits of these approaches is beyond the scope of this article, although suffice to say that analytical approaches for small sample studies (often the case in human experimentation) using full Bayesian, quasi-Bayesian and frequentist decisions must be well justified, reported transparently and interpreted correctly.

Practical Implementation

Practical implementation of research paradigms in the field with athletes and sports is often a challenge. Our research group developed a model of salivary IgA concentration as a marker of the risk of upper respiratory tract illness during the 1990's [6]. Although there is still merit in this approach with athletes, implementation has proved challenging in the field. A substantial number of studies have been published on exercise and salivary IgA, and variable outcomes can dilute confidence in interpreting results. Difficulties in standardisation of specimen collection, storage and handling of samples, and laboratory- and field-based quantification are often experienced [6]. Moreover, the cost of biomedical testing is significant for many sports and nations. Diagnostic testing still forms the majority of work, although technological advances and further research should facilitate an increase in monitoring and intervention before athletes present with symptoms of illness. The advent of small portable point-of-care analysers is promising. However, researchers, clinicians and team support personnel have to be mindful of calibration, reliability and validity of instruments irrespective of their size and portability. Translation of quantitative algorithms and references ranges, and how those values might vary between field and laboratory settings are current research foci.

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TRAIN THE LYMPHOCYTE! EXERCISE AFFECTS T CELL LIFE CYCLE THROUGHOUT LIFE

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Key words: hematopoiesis, progenitor cells, apoptosis, cytokines, immunosenescence

T cells life cycle begins with hematopoiesis, a process in which all red blood and immune cells are generated. Hematopoiesis mainly occurs within the bone marrow (BM) and, under certain conditions, in peripheral tissue compartments such as spleen. Regarding the development of lymphocytes, their progenitors are known as hematopoietic stem and progenitor cells (HSPCs). Function, differentiation, and mobilization of these self-renewing and pluripotent cells is mainly regulated by the secretome of mesenchymal stromal cells in the bone marrow niche through release of cytokines and hematopoietic growth factors. Acute exercise transiently mobilizes progenitor cells into the circulation. Thereby, numbers of HSPCs in BM remains stable because both acute and chronic exercise training also stimulate proliferation of HSPCs to ensure a stable HSPC number in the BM compartment. Highest mobilzing effects were shown in response to acute and intensive endurance exercise bouts. Mediators of exercise-induced progentor cell mobilization are the increased expression of granulocyte colony-stimulating factor (G-CSF), stem cell factor, vascular endothelial growth factor (VEGF), angiopoietin-1, and the interaction of CXCL4 and stromal derived factor 1 (SDF-1) (1,2). In response to regular exercise training, it is suggested that HSPC quantity, availability, and colony-forming capacity is stimulated suggesting an important function of these cells for regeneration and adaptation of the immune system and potentially other organs and tissues. While direct exercise effects on differentiation stages from HSPCs to common lymphoid progenitors and differentiated lymphocytes remain to be shown, it is suggested that the increased release of HSPCs into circulation relatively increases the circulating pool of lymphocytes which shows tendencies to be higher in regularly active individuals compared to sedentary subjects (2,5).

During normal conditions, the circulating pool of T cells is differentiated during the gradual release of naive cells from the thymus. Thymic output is more efficiently during young life followed by a progressive involution of this organ. Accordingly, the release of naive T cells declines to low levels during aging. Subsequently, the relative amount of terminally differentiated cells and clones of viral specific T cells increases throughout life. This aging processes are assumed to increase susceptability to infection with novel pathogens in older individuals and was demonstrated to represent a clinical relevant immune risk factor during aging (1,4,5). Some data from animal studies indicated that regular exercise slightly restores thymic function. Accordingly, exercise training increases the relative amount of naive T cells and lowers proportions of terminally differentiated $CD4^+$ und $CD8^+$ T cells. Murine studies indicated that these processes might not only account for blood lymphocytes, but also for splenic T cells. During each bout of acute exercise primarily senescent T cells are mobilized into the circulation making the contact with potentially apoptosis-inducing factors like reactive oxygene species (ROS) more probably. Accordingly, exercise seem to stimulate programmed cell death process mainly in highly differentiated and senescent T cells. Some studies indicated that apoptotic processes create signals for the production of HSPCs to produce naive T cells. Mediators of this increased cell-turnover might be microparticles, such as apoptotic bodies, which represent signaling molecules expressed by dying cells (3,4).

$CD4^+$ cells are important cytokine producers which can be further subdivided into Th1 and Th2 cells. Th1-type cells tend to produce mainly potent proinflammatory cytokines like interferone-γ, while Th2 cells express cytokines which evoke antibody responses or anti-inflammatory cytokines such as IL-10. Moderate bouts of exercise affect Th1/Th2 balance by increasing relative proportion of Th2 cells in blood. This process is supported by the increased appearance of regulatory T cells (T_{regs}, $FoXP3^+$) in blood of regularly active subjects. Both processes are assumed to affect the anti-inflammatory potential of exercise training. Exercise also stimulates the vascular egress of effector T cell subtypes followed by redistribution of cells into periperhal sites of antigen encounter like lungs and gut (1,3,4). Thereby, exercise training seems to stimulate also several functional aspects of T cells like intracellular calcium signals and immunometabolism such as glutamine, β-alanin, and glucose metabolic pathways. During aging, an accumulation of T cells which express markers

of immunosenescence is documented. Exercise seems to delay immunosenescence by an increase of $CD28^+$ cells in active elderly subjects. In addition, telomere lengths of T cells from trained subjects seem to be longer compared to untrained subjects leading to an increased proliferation capacity of these cells (4,5).

Taken together, acute or chronic exercise seem to affect T cell life cycle during genesis, differentiation and maturation, and aging. Nearly almost these adaptations seem to positively stimulate immune function as long as exercise is performed at moderate intensities and regularly. While many aspects of the effects of exercise on the differentiated T cell subpopulations remain to be shown, others seem to be represent a robust physiological basis for the lower susceptibility to infections of regularly active people.

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IMMUNE RESPONSES TO EXTREME CHALLENGES

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Key words: Training, Psychological stress, Sleep, Environment, Nutrition

Numerous studies over the last 30 years indicate a decrease in immunity and an increase in upper respiratory infection (URI) symptoms in athletes and soldiers.

Experts attribute these observations to the various stressors associated with both athletic training and competition (e.g. heavy exercise, nutritional deficits) and military training and field manoeuvres (e.g. sleep disruption and environmental stress) (18). Psychological and physical stressors have long been known to influence the sympathetic-adrenal axis and pituitary-adrenal axis since the pioneering work of Walter B Cannon (coined 'fight or flight' response) and Hans Selye (coined term 'stress') in the 1930s. These common pathways and shared effector limbs for the body's response to stress in its many forms give rise to increases in circulating catecholamines and glucocorticoid hormones; these hormones are widely acknowledged to have immunomodulatory effects. This presentation will provide new insights about, and recommendations for coping with, the effects of extreme challenges that athletes, soldiers and others encounter on immune health; including, the effects of heavy training stress, life stress, sleep disruption, environmental stress and nutritional deficits.

Heavy training stress

In athletes under heavy training both innate and acquired immunity are often observed to decrease after heavy exertion, typically 15─25%: prolonged heavy training sessions (> 90 min) and periods of overreaching and maladaptation in particular have been shown to decrease immunity (5, 13). Whether the observed changes in immunity with acute heavy exercise and heavy training are sufficient to increase URI susceptibility remains a point of contention. Recent work indicates that high level athletes are particularly susceptible to URI symptoms during periods of intensified training in the winter (9). As such, when scheduling the training programmes of athletes and soldiers, coaches and commanders need to be mindful of the decrease in immunity associated with very prolonged exercise bouts, periods of high training load and when implementing increments in training load.

Life stress

Given the well-known and marked influence of psychological stress on immunity and infection resistance (4), and the shared pathways and effector limbs for the body's response to various stressors (e.g. exercise, psychological stress) it stands to reason that psychological stress plays a role in the decrease in immunity with prolonged heavy exercise and heavy training (15, 19). Unfortunately, exercise immunologists

rarely report measures of psychological stress in their studies and so there is little by way of empirical evidence to support this contention. It's quite conceivable, that psychosocial stress status in high level athletes and soldiers (related to life stress, competition or operations, injury, travel, sleep disruption, jetlag etc.) accounts at least in part for the influence of acute exercise and heavy training on, immunity and host defence (19). This presentation will make a call to exercise immunologists to account for psychological stress when examining the immune response to exercise; also, for coaches and support staff to monitor psychological wellbeing alongside more traditional physiological measures of training stress. Accordingly, very recent evidence highlights that aspects of mental health such as depression and psychological stress are important risk factors for illness in Olympic athletes (6). Studies are required to demonstrate the utility of interventions to reduce psychological stress in athletes and soldiers experiencing high psychological stress in order to optimise immunity and host defence.

Sleep disruption

Like the other forms of stress discussed, sleep disturbances influence immunity via activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous-system (14). Chronic sleep disturbance and disruption to the normal circadian rhythm are associated with inflammation and desynchronization of rhythmic immune variables. These responses likely contribute to increased risk of infection, cardiovascular disease, and cancer in long-term shift workers. Not only do soldiers experience sleep disruption (e.g. during sustained operations), there is now evidence that athletes experience poor sleep patterns compared with non-athletes. This presentation will highlight what little we know about how sleep disturbance influences the immune responses to exercise. Compared with normal sleep, a disrupted night's sleep appears to prime the immune system and enhance immune-surveillance by stimulating total lymphocytes, $CD8^+$ T cells, NK cells, and $\gamma\delta$ T cells to leave the blood and migrate to potential sites of infection during the early recovery period after exercise (10). By contrast, other studies indicate that a night without sleep does not influence leukocyte trafficking, neutrophil degranulation, or mucosal immunity at rest or after exercise (14). Subtle immune changes have been observed after a night without sleep, including a shift toward a T helper 2 cytokine profile (11).

It is uncertain whether these subtle immune modifications with acute sleep loss are clinically meaningful for the athlete or soldier (14). When considering the potential effects of poor sleep on immunity in athletes and soldiers, it is important to distinguish between acute and chronic sleep disturbance. Chronic sleep disturbance (12 nights, 50% sleep loss) increases the plasma inflammation markers C-reactive protein and IL-6 (8). However, intervening daytime naps can counter this apparent inflammatory response (17). Short sleep duration (<7 h/night for 7 d) decreases the response to hepatitis B vaccination and the likelihood of clinical protection (16). Similarly, a night of wakefulness after hepatitis A vaccination decreases the specific antibody response 2–4 months later (12). People who experience poor quality sleep and/or regular sleep deprivation also have a 4–5-times greater risk of developing the common cold (3). Continued research efforts should be directed towards monitoring and improving sleep in athletes and soldiers and understanding the implications for immune health.

Environmental stress

This presentation will cover the controversial beliefs held by many athletes that breathing cold, dry air and getting a 'chill' through cooling of the skin cause the 'common cold'. Although controversial, some evidence shows that peripheral cooling of the nose and upper airways (and even the feet) can increase common cold symptoms, possibly by inhibiting immune cell trafficking and creating a suitable local environment for viral replication (7). Although not entirely conclusive, evidence indicates that cold exposure often precedes, and is associated with increased incidence of, URIs including the common cold (19). Other controversies discussed in this presentation include whether exposure to environmental extremes (e.g. heat acclimation, cryotherapy and hypoxic training) compromises immunity and increases URI in athletes and soldiers. With the exception of cell-mediated immunity that tends to be decreased, exercising in environmental extremes does not appear to provide an additional threat to immunity and host defence. Recent evidence suggests that immune health may actually be enhanced by regular intermittent exposures to environmental stress e.g. intermittent hypoxia training (20).

Nutritional deficits

Nutrient availability can influence immunity directly because macro- and micro-nutrients are involved in a multitude of immune processes (e.g. as a fuel source) but also indirectly via increases in stress hormones during prolonged exercise e.g. when blood glucose falls. Athletes and soldiers either intentionally or non-intentionally experience deficits in energy intake (e.g. extreme weight-loss diets, restricted rations) and macronutrient intake (e.g. restricted carbohydrate). For example, soldiers on a 12-day training exercise in the tropics who received only half of their estimated energy intake in ration packs experienced decreases in both cellular and humoral immunity (2).

Paradoxically, nutritional strategies currently adopted by endurance athletes, including training with low carbohydrate, may benefit training adaptations and performance at the expense of immunity; for example, carbohydrate restriction may increase the immunosuppressive stress hormone response to exercise (1). As such, the rather modest benefits studies show in terms of training adaptations and performance might, in the long term, be lost if the athlete gets sick more often. Studies are required to investigate whether the nutritional practices adopted by elite athletes impair immunity and increase infection; and, whether purported 'immune-boosting' supplements benefit immune health for athletes and soldiers without blunting the desired training adaptations.

This presentation highlights the effects of extreme challenges that athletes, soldiers and others encounter on immune health. Interested readers are directed to recent reviews on the topics covered in this presentation (1, 14, 19).

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IMMUNE CELL REGULATION BY MUSCLE CELLS: RESPONSES TO CONTRACTION AND HIGH FATS

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Key words: myotube contraction; saturated fatty acids; myokines; monocyte chemoattraction

Obesity-induced insulin resistance and its consequent type 2 diabetes correlate with by whole body low-grade inflammation and a gain in pro-inflammatory macrophages in the expanding adipose tissue. Yet, skeletal muscle is the tissue determining insulin-dependent glucose disposal and hence the insulin response of muscle is key to whole-body insulin resistance. Therefore we asked whether skeletal muscles undergo macrophage infiltration during obesity and if so, by which mechanism. Our first two aims were to determine whether skeletal muscle gains pro-inflammatory macrophages in mice fed high fat diet (enriched in saturated fats), and whether myotubes grown in cell culture would respond to saturated fat exposure by attracting monocytes.

Exercise is a major strategy to improve whole-body insulin action, causing changes in skeletal muscle metabolism and requiring immune cell participation to aid in

ongoing muscle repair, but the cues emanating from the working muscle that attract monocytes were not fully understood. Hence, our third aim was to investigate how contracting myotubes would impact on immune cells.

In mice, three days of high fat feeding sufficed to elevate skeletal muscle markers of inflammation (TNF□, CCL2) and by 1 week pro-inflammatory macrophages ($CD11c^{+}$,$F4/80^{+}$) were elevated in the tissue, .with total macrophages representing 55% of the immune cell population within the tissue. Similarly, glucose intolerant obese individuals with documented insulin resistance of muscle showed higher Cd68 and CD11 expression compared to similarly obese but glucose tolerant individuals, which correlated with whole-body insulin resistance. Conversely, across all patients, whole-body insulin sensitivity correlated positively with gene markers of anti-inflammatory macrophages.

In myotubes in culture, exposure to the saturated fatty acid palmitate (PA) increased cell-autonomous gene expression of CXCL2, CCL2, IL-1□, TNF□, IL6 whereas there was no effect of the monounsaturated fatty acid palmitoleate (PO) of equivalent carbon chain length. PA-treated myotubes chemoattracted monocytes and this was mediated via ATP release from myotubes, liberated through pannexin channels. PA treatment elevated the expression of pannexin-3, downstream of NF□B activation. PA-treated myotubes also polarized macrophages towards a more pro-inflammatory orientation.

Electrical pulse stimulation (EPS) induced myotube contraction and medium from these myotubes attracted monocytes, but in this case the chemoattracting factor is a protein. EPS also increased glucose uptake into the contracting myotubes, but this response was independent of exogenously secreted factors. In contrast, short-term tetanic contracture of myotubes released ATP via existing pannexins channels that acted autocrinely to promote glucose uptake. Hence, depending on the strength and type of muscle contraction/contracture, myotubes regulate their metabolism, and possibly the immune system, by distinct mechanisms.

Overall, our studies reflect the intense communication between the muscle metabolic state and surrounding immune cells.

MACROPHAGES DURING SKELETAL MUSCLE REGENERATION: FROM EXPERIMENTATION IN MOUSE TO HUMAN PHYSIOLOGY

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Key words: Muscle regeneration, inflammation, macrophages

Inflammation after a tissue damage encompasses several sequential phases including: (1) the mounting of the inflammatory response, characterized by the infiltration of immune cells to the site of injury and the release of proinflammatory effectors; (2) the resolution of inflammation, characterized by a shift from a proinflammatory environment to the establishment of the anti-inflammatory phase of inflammation; and (3) tissue repair/regeneration including angiogenesis, matrix remodeling and return to homeostasis. Almost all immune cell types participate in this inflammatory process. However, macrophages are present in high number and during all the sequences of the inflammatory response. Because of their high versatility and their impact on their environment, they sustain both the mounting and the dampening of the inflammatory response. Accumulating lines of evidence of the beneficial—and pleiotropic roles—of macrophages in tissue repair indicate that inflammation should not be considered as a bad or detrimental process. Conversely, it should be viewed as a dynamic process of which sequential steps must be tightly coordinated in space and time to be fully efficient to support skeletal muscle regeneration.

Most of the knowledge on the role of inflammation during skeletal muscle regeneration comes from mouse experimental models that use toxic injury. Although not physiologically relevant, this type of injury offers the advantage of being highly reproducible, the kinetics of each step of muscle regeneration being well characterized. Moreover, these models are highly inflammatory, which is useful to study inflammation.

The overall role of macrophages during skeletal muscle regeneration will be presented, as well as the sustaining molecular mechanism of their own regulation and the regulation of myogenesis. Then, some elements will be presented to open

the discussion on the link between the knowledge obtained from experimentation in small animals and human physiology, notably in the context of Exercise-Induced Muscle Injury (EIMD).

PROFILING SKELETAL MUSCLE INJURY AND REGENERATION USING PROTEOMICS

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Key words: muscle injury, inflammation, necrosis, regeneration, proteome signature, network analysis

Muscle contusion injuries are relatively common in contact sports, workplace and vehicular accidents. They are associated with significant acute necrosis and inflammation, followed by regeneration over 2□4 weeks. Muscle contusion injuries have been characterised using histology, immunohistochemistry and some molecular techniques. However, few studies have employed global proteomics profiling to investigate the time course of changes in the protein composition of muscle in the different phases of tissue destruction, repair and remodelling. Mass spectrometry based proteomics offers some key analytical benefits, including the ability to catalogue a large number of proteins and establish comprehensive biomarker signatures that represent important physiological processes. We induced muscle contusion injury in anaesthetised rats by dropping a cylindrical 400 g weight on the hind limb, in the region of the gastrocnemius muscle. The rats were then allowed to recover for 6 h, 12 h, 1, 3, 7 or 14 d before they were sacrificed (n=5 per time point). A control group of n=5 non-injured animals was also included. The gastrocnemius was removed and snap frozen in liquid N2. Around 50 mg of muscle tissue were dissected and placed in a microcentrifuge tube for homogenisation, sonication and

protein extraction. Samples were centrifuged to collect the supernatant, and the protein concentration was measured. A pooled sample prepared with muscle from all of the animals was divided in two and fractionated by LDS-PAGE and OFFGel electrophoresis. Subsequent fractions were digested using in-gel digestion or the filter-aided sample preparation (FASP) technique, respectively. All 35 individual samples were digested by FASP. Liquid chromatography tandem mass spectrometry (LC-MS/MS) analysis was performed. Fractions of pooled samples were analysed by data-dependent acquisition, whereas each individual sample was analysed by data-independent acquisition. A peptide-spectrum identification search using a UniProt rat database was performed on all the data from fractionated samples through ProteinPilot software, which identified around 2,000 different proteins in the muscle homogenates. The over-represented biological processes, molecular functions, and cellular components were determined through Gene Ontology (GO) enrichment analysis of the whole muscle proteome, using the BiNGO app within Cytoscape (Version 3.4.0). The top biological processes included cellular metabolic processes, catabolic processes, translational elongation, electron transport chain, oxidation/reduction and cellular respiration. The top molecular functions included protein binding, catalytic activity, oxidoreductase activity, translation factor activity, nucleotide binding and hydrolase activity. The top cellular components included the cytoplasm, cytosol, mitochondrion, organelle and protein complex. Data analysis is ongoing to establish a temporal profile of quantitative changes in biological processes, molecular functions and cellular components during the phases of muscle tissue destruction, repair and regeneration.

RUNNING FROM CANCER: A ROLE FOR EXERCISE-MEDIATED CONTROL OF CANCER THROUGH REGULATION OF IMMUNE FUNCTION

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Key words: Exercise; physical activity; inflammation; NK cells; tumor growth

Introduction

The benefits of engaging cancer patients in an active lifestyle and exercise training despite their cancer disease are becoming increasingly evident. At present, more than 100 exercise intervention studies in cancer patients have reported favorable effects on both patient-reported outcomes and physical functioning, when exercise is performed during or after anti-neoplastic therapy (1). Moreover, early evidence from observational studies has shown that physical activity reduces the risk of disease recurrence in colorectal, prostate and breast cancer patients (2-4), suggesting that exercise has a direct effect on tumor growth.

In addition to the clinical training intervention studies, a number of preclinical studies have shown that exercise training can directly affect tumor growth. To this end, more than 80 different preclinical studies in rodents have investigated the impact of exercise on tumor incidence and tumor growth, and the vast majority of the studies shows that voluntary wheel running, treadmill running or swimming can reduce tumor growth in rodents (5). Yet, in order to further elucidate that basis for this training-dependent suppression of tumor growth, understanding of the underlying molecular mechanisms is warranted.

Control of tumor initiation and growth through exercise-dependent regulation of cytotoxic immune cells

We have recently shown that voluntary wheel running in mice could reduce tumor growth with 50-60% across a range of genetic and transplantable murine tumor models (6). This exercise-dependent suppression of tumor growth was associated with an increase in intratumoral immune cell infiltration, in particular of cytotoxic natural killer cells (NK) and T cells. To explore the importance of this enhanced immune cell infiltration, we repeated the voluntary wheel running studies in mice depleted of NK cells or mice lacking T cells. While the more than 50% reduction in tumor growth with wheel running persisted in mice lacking T cells, this exercise-dependent suppression of tumor growth was completely abolished in mice depleted of NK cells. These results highlight the pivotal role of NK cells in driving the exercise-mediated suppression of tumor growth.

We went on to characterize how wheel running regulated intratumoral immune cell infiltration (6). First, NK cells are mobilized to the circulation through increased blood flow and epinephrine induction during exercise (7). In line with this, blockade of β-adrenergic signaling during the exercise intervention blunted the exercise-mediated tumor suppression and immune cell infiltration into the tumors of the running mice. In addition, we found that wheel running increased the immunogenic profile of the tumor and redirected trafficking of the mobilized immune cells into the tumors through an IL-6-dependent mechanism. IL-6 is released from contracting muscles during exercise, and this muscle-derived myokine release points to a role for muscle to immune cell cross talk during exercise (6).

Translability to cancer patients

While this preclinical study was the first to link exercise to cancer control through mobilization of cytotoxic immune cells, it has long been recognized that exercise regulate immune cell mobilization in humans. Based on an extensive amount of studies in humans, a consistent picture of a rapid and general mobilization of NK cells during exercise is evident (7). While NK cells are the most responsive immune cells to the exercise-dependent mobilization, cytotoxic T cells and to a lesser extent B cells are also mobilized to the circulation during exercise. This exercise-dependent mobilization relies on β-adrenergic signaling, thus the performed exercise must be of an intensity associated with increases in catecholamine levels and heart rate to elicit this response (7). Once mobilized, these cytotoxic immune cells survey the body for transformed cells as immunological targets.

The consistency of the exercise-dependent mobilization of immune cells, in particular NK cells, is highlighted by the fact that this response is observed across all ages and in both genders, as well as in lean and obese individuals, and trained and inactive people. In fact, any variation in the exercise-dependent NK cell mobilization response is more likely to reflect a barrier in exercise performance than a functional deficit in NK cell mobilization. Despite the general understanding of immune cell mobilization with exercise, very little is known in cancer patients. Only one study has characterized the acute mobilization of NK cells, and finds that breast cancer survivors are able to mobilize NK cells equivalent to that observed in age-matched control subjects (8). Yet, the study also documented that the resting levels of NK

cells were slightly reduced in the breast cancer survivors due to preceding chemotherapeutic therapy (8). We have studied immune cell mobilization in patients with cancer in the esophageal-gastric junction receiving neoadjuvant chemotherapy. These patients are generally more fragile and symptom-ridden that the breast cancer survivors, yet our experience show that these patients can also mobilize large amounts of cytotoxic immune cells. In fact, 35 min of interval-based cycling induced a 3-7 fold increase in circulating NK cells (unpublished data).

Making tumors more immunogenic

The clinical potential of exercise-mediated immune cell mobilization is emphasized by the huge focus on cancer immune therapy. Currently, the introduction of immune therapy in cancer therapy is revolutionizing the treatment of cancer patients (9). Immune check point blockers can relieve the brake that some tumors are placing on cytotoxic immune cells by interfering with the immune check point receptor-ligand interaction (e.g. PD-1 and PD-L1). Clinical insight from the first trials with these drugs show that the immune check point blockers are most efficient if the tumors are highly immunogenic. Thus, approaches aimed at generating an inflammatory intratumoral environment may promote the efficacy of these drugs. In the tumors from the above-mentioned study (6), we found that voluntary wheel running delivered such therapeutic adaptations within the tumors, as we observed an exercise-dependent regulation of the expression of various immune check point receptors, chemokines and cytokines, all adding to the observed enhanced immune cell infiltration. Thus, exercise supports cancer patients' immune function and may reinforce the effect of immunotherapeutic strategies. This demonstrates how insight into the mechanistic effects of exercise might govern the use of targeted exercise in combination with conventional treatments. However, this field is only just starting to attract attention and far more research is warranted to fully understand the synergistic effects of exercise and different modalities of anti-cancer therapies.

Conclusion

Our results underline that molecular and systemic changes occurring during exercise can directly target cancer cells, controlling their initiation and progression. Our results demonstrate that an exercise-mediated mobilization and activation of cytotoxic immune cells, in particular NK cells, plays a pivotal role in this control of tumor

growth. If these exercise-dependent molecular and immunogenic effects can also regulate direct anti-cancer effects in cancer patients, incorporation of exercise therapy into standard oncological treatment is highly warranted. Conceptually, this place exercise training within anti-cancer treatment strategies, rather than the current focus of exercise as supportive care and rehabilitation for cancer patients.

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LESSONS FROM NATURAL KILLER DEFICIENT PATIENTS – IMPLICATION IN EXERCISE IMMUNOLOGY

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Key words: natural killer cell deficiency, herpes family virus, trafficking

Natural killer cell was found as large granular lymphocyte, a distinct subset of lymphocytes exhibiting antigen independent killing of leukemia cells and virus infected cells. NK cells had long time been one of the main focuses of research in exercise immunology because intensity or duration exercise largely influence the number and the function of NK cells in the blood sample, and because the cytotoxicity was not restricted to a specific antigen. The early findings lead to the assumption of the well-known open window theory. The efforts, however, of elucidating the mechanism of NK cell recognition of target cells reached to the conclusion that the recognition is indeed highly specific but antigen independent. Both altered-self theory and missing-self theory were successful in defining the molecular mechanism of target condition principally regulated by the modulation of class I major histocompatibility antigen (MHC-I) expression on the target. The cytotoxicity of NK cell is further determined by corresponding NK cell receptors, some of which inhibit the killing response (killer inhibiting receptor: KIR) and some activating the killing process (killer activating receptor: KAR), and the consequence seems to be determined by the balance between target bound KARs and KIRs.

Clinical findings of natural killer deficient patients

The progress in elucidating the mechanisms of NK cells enabled clinical scientists to better characterize immunodeficiency syndromes. A NK cell deficient patient within a family was reported in 1989 by Biron et.al. (Biron et al., 1989) Several types of NKD have been characterized; NKD lacking NK cells at all or NKD lacking functional

molecules. A common feature among various NKD patients is that they all are susceptible to infection of herpes virus including varicella zoster virus (VZV), Herpes simplex virus (HSV) I and II, Epstein Barr virus (EBV), and cytomegalovirus (CMV) and occasionally papilloma virus often leading to severe to fatal outcome (Orange, 2013). This fact clearly demonstrates that NK cells have distinct role in the protection of herpes viruses exhibiting lower cytotoxicity in the initial phase of infection. The most effective therapeutic approach for these patients lacking NK cells is considered as bone marrow transplantation to reconstitute their NK cell defense system.

Another relevant study to understand the role of NK cells is a 11-year cohort study with setting cancer incidence among 3625 community-dwelling adults over the age of 40 by Imai et al (Imai et al., 2000). They found a significant association between baseline NK cell activity grouped in tertiles and cancer incidence and mortality over 11 years among 3625 community-dwelling adults over the age of 40. There was no significant difference in cancer incidence or mortality between the highest NK cell activity tertile and the mid tertile groups. The lowest tertile group, however, had a significantly higher mortality rate of cancer. The study is the first population study suggesting the role of NK cells in tumor surveillance, and suggests there is a distinct population who have lower NK cell activity with higher risk of cancer.

Implication in exercise immunology

Considering the protective role of NK cells in herpes family viruses, question arises whether herpes gladiatorum, a common skin infection among wrestlers (Anderson, 2003), or EB virus reactivation among elite swimmers (Gleeson et al., 2002) involve transiently impaired NK function due to strenuous training. Similar to other types of strenuous exercise, wrestling training resulted in a marked increase in the circulating number of NK cells. This altered trafficking of NK cells during strenuous exercise may largely depend upon catecholamine released during exercise. Both marked increase during exercise and marked decrease after exercise in the circulating number of NK cells may reflect altered trafficking without modifying the total pool of NK cells (Zhang et al., 2006). Whether this altered distribution, previously considered as an open window, has a role in the high prevalence of skin infection among the wrestlers or EB reactivation in elite swimmers is unknown.

Changes in the distribution of NK cell subtypes (mature and immature) during and after exercise are reported, but the length of changes required for altered susceptibility or severity of herpes family virus infection is unknown. Examination of herpes family virus infected cells for the expression of KAR (most commonly NKG2D) ligands such as MICA, MICB and ULBPs, which trigger NK cell activation upon binding to KARs and trigger inhibition upon binding to inhibitory KIRs may give a clue to the presence of open window during and after strenuous exercise. It must be noted that herpes family virus infection is known to epigenetically modulate the expressions of KARs and KIRs ligands of the infected cells suggesting the strategy of viruses to escape from the human immune system (Schlums et al., 2015). Whether hormonal changes or changes in sympathetic activity confer expression patterns of KARs and KIRs on herpes family virus infected cells is still unknown.

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IMPACT OF NUTRITION ON METABOLIC AND IMMUNE SYSTEM RECOVERY FROM HEAVY EXERTION: VALUE OF MULTI-OMICS APPROACHES

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Key words: Immunometabolism, metabolomics, polyphenols, carbohydrate, immunonutrition support, inflammation

Immune response to intensive exercise, overreaching, and overtraining

Athletes participating in one bout of prolonged and intensive exercise such as marathon and ultramarathon race events experience acute physiological stress reflected by muscle microtrauma, oxidative stress, and systemic inflammation. Concomitant with these stressors are widespread perturbations in innate and adaptive immunity including decreases in natural killer (NK) cell cytotoxic activity, granulocyte respiratory burst activity, nasal and salivary IgA (sIgA) secretion, delayed type hypersensitivity, and mitogen-induced lymphocyte proliferation, as well as extensive alterations in circulating immune cell populations. This period of decreased host protection is often followed by elevated rates of upper respiratory tract infections in the athletes 1-2 weeks after competition.

Metabolomics, lipidomics, proteomics, and immunometabolism relationships

Heavy exertion has a profound, acute effect on human metabolism, but most studies have focused on a small, targeted number of biochemical outcome measures. The recent development of metabolomics profiling technologies provides a system-wide

view of the metabolic response to exercise by simultaneously measuring and identifying a large number of small molecules. Metabolomics, lipidomics, and proteomics data from sports nutrition based studies have the potential to shape a new generation of integrative studies using metabolite measurements with immunology, molecular epidemiology, genomics, transcriptomics, and proteomics.

Seminal papers using the latest multi-omics technology indicate that heavy exertion has wide ranging, substantial, and prolonged influences on lipid and protein metabolism, marked by increases in metabolites related to carnitine metabolism and long chain, dicarboxylate, and essential fatty acid metabolism, and proteins related to immune function (half of the proteins expressed after heavy exertion are immune-related). Perturbations in many of these metabolites and proteins are still apparent in endurance athletes after 14 h of recovery. Carbohydrate intake strongly attenuates the magnitude of increase in exercise-induced metabolites from the lipid super pathway, and the rate of recovery to pre-exercise levels is quicker.

Immunonutrition strategies

The unexpected discovery during the 1990s that carbohydrate ingestion influenced the acute immune response to prolonged and intense exercise inspired a new line of research in the area of nutrition-exercise immunology. Nutritional components and products of every conceivable category have been tested for their capacity to attenuate post-exercise inflammation and immune changes, with a focus on the nonspecific, innate arm of the immune system. The primary hypothesis is that the risk of immunosuppression and respiratory illness is more effectively countered if the nutritional agent augments post-exercise natural killer cell, macrophage, and granulocyte function in comparison to the slower moving adaptive immune system.

Unfortunately, except for carbohydrate, results have been disappointing, although some would argue that much remains to be studied and discovered (in particular, the myriad polyphenols) in the fledgling field of nutrition-exercise immunology. At this time, data from exercise-immune studies are non-supportive, mixed, or of limited clinical, countermeasure significance for use of various products including anxtioxidants, N-acetylcysteine, vitamins and minerals, glutamine and other amino acids, protein, beta-glucans, fish oil, alpha-linoleic acid, probiotics, bovine colostrums, ginseng, Echinacea, and other nutritional components. The proposed

benefits of antioxidant supplementation in attenuating oxidative stress and immune dysfunction during exercise remain unsubstantiated, and may work contrary to expectations, as highlighted by the finding that large dose vitamin E supplementation amplified post-race inflammation and oxidative stress in Kona Ironman athletes. Glutamine is essential for optimal immune function, and a popular rationale for glutamine (and many other nutrients) is that higher than normal intake is needed to counter exertion-related demands from the immune system. However, glutamine supplements are not recommended because the best studies show no benefits when compared to placebo, perhaps due to abundant storage pools within the body that cannot be sufficiently depleted by exercise.

Carbohydrate

A series of studies dating back to the mid-1990s showed that ingestion of carbohydrate supplements (30-60 g/h) during prolonged, intensive exercise attenuated increases in blood neutrophil and monocyte counts, granulocyte phagocytosis, stress hormones, and anti-inflammatory cytokines such as IL-6, IL-10, and IL-1ra. At the same time, however, null effects of carbohydrate ingestion were measured for exercise-induced decrements in naturally killer cell lytic activity, salivary IgA output, and T lymphocyte proliferative capacity. Thus, carbohydrate ingestion emerged as an effective but partial countermeasure to immune dysfunction during recovery from heavy exertion.

Carbohydrate may exert these impressive countermeasure effects through multiple mechanisms including an elevation in blood glucose and tissue glucose uptake leading to diminished central nervous system activation and stress hormone output, decreased cytokine mRNA expression, lower beta-oxidation of lipid fuels, reduced pro-inflammatory signals, and attenuated IL-6 release from the working muscle tissue. Exercising with higher blood glucose levels decreases hypothalamic-pituitary-adrenal activation, leading to moderated release of adrenocorticotrophic hormone and cortisol, growth hormone, and epinephrine. Stress hormones have an intimate link with genes that control cytokine production, and the function of multiple cell types of the immune system. Exercise-carbohydrate interactions, especially during exercise and the early post-exercise recovery period, may modulate signal transduction cascades that influence protein regulatory systems. Thus there is a

strong rationale for providing carbohydrate as a countermeasure to exercise-induced inflammation when body carbohydrate stores are challenged. Perhaps just as importantly, studies consistently show a 2 to 6% improvement in performance by athletes ingesting carbohydrate compared to water during intensive exercise bouts lasting longer than two hours.

The value of using carbohydrate and other types of immunonutrition support for athletes has been questioned because blocking transient post-exercise elevations in inflammation, oxidative stress, and stress hormones may interfere with important signaling mechanisms for training adaptations. The literature is limited and not consistent in this area, however, especially in regards to combining carbohydrate intake with heavy training. Training with limited carbohydrate availability may lead to some improved metabolic adaptations, but studies have been unable to link this with performance improvements. Part of the problem is that training with limited carbohydrate is difficult, leading to decreased intensity and duration. One argument is that carbohydrate ingestion only partially lowers post-exercise inflammation and stress hormones, analogous to the beneficial use of ice packs to “take the edge off” swelling following mild injuries. In the end, the value of carbohydrate and other forms of immunonutrition support for athletes during periods of heavy exertion and competitive races should be evaluated by whether or not the athlete has improved recovery, lowered illness rates, reduced muscle damage and soreness, and enhanced overall athletic performance.

Polyphenols

Due to their pleiotropic properties and structural diversity, polyphenols have created much interest as potential countermeasures to exercise-induced physiological stress. The 8,000 phenolic compounds are divided into four main classes, including the six sub-classes of flavonoids that comprise nearly 50% of all polyphenols. Improved assessment techniques have led to many recent publications that support a strong and impressive linkage between high versus low dietary polyphenol intake and reduced risk for overall mortality, a wide spectrum of chronic health conditions, systemic inflammation, and acute respiratory illness. Flavonoids exert anti-viral effects, modulate natural killer (NK) cell activities and regulatory T (Treg) cell properties, and influence macrophage inflammatory responses.

Most polyphenols, however, are poorly absorbed in the human small intestine and undergo extensive biotransformation after ingestion. A large proportion of ingested plant polyphenols reaches the colon, and microbial degradation produces gut-derived phenolics that can be reabsorbed into the systemic circulation, exert a variety of bioactive effects, and then finally be excreted in the urine. Thus most studies incorporate a 1-6 week loading period prior to an exercise stress intervention to allow sufficient time for body tissues to adapt to the higher phenolic flux level. Although there are indications that the biotransformed, gut-derived phenolics exert anti-inflammatory and anti-viral effects, these bioactive influences are subtle and become clinically important over long time periods. Dosing strategies (duration, frequency, amount, timing) are still being explored, and supplements vary from single and combined purified polyphenols (e.g., resveratrol, quercetin), to plant extracts (e.g., black currant, bilberry, green tea) and increased fruit and vegetable food or juice intake (e.g., bananas, tart cherry juice, fresh blueberries). A common finding thus far is that polyphenol-rich plant extracts or supplements have small but significant effects in increasing anti-oxidant capacity, with inconsistent, short-term effects on exercise-induced oxidative stress, inflammation, and immune dysfunction. High blueberry and green tea flavonoid versus placebo intake for 17 days was linked to reduced ex vivo viral replication in blood samples collected from athletes after a 3-day overreaching, running protocol. Long-term studies are needed to better understand the potential benefits of increased polyphenol intake for athletes during periods of intense training. Polyphenols may serve as a useful substitute for ibuprofen, a drug which blunts early translational signaling responses in human skeletal muscle and amplifies post-exercise inflammation.

Conclusions

In general, exercise activates multiple molecular pathways, many involving the immune system, and these are sensitive to nutritional influences (e.g., the inverse relationship between carbohydrate supplementation and post-exercise plasma IL-6 levels). Multi-omics-based approaches are particularly useful in interpreting human responses to nutritional manipulation within the exercise context, and improves the capacity to capture complex and subtle influences on whole body metabolism and physiology. Future studies using multi-omics approaches will help determine if

increased long-term intake of high carbohydrate-polyphenol food sources is an effective immunonutrition support strategy for athletes.

CAN NUTRITIONAL SUPPLEMENTS HELP EXERCISE-INDUCED IMMUNODEPRESSION?

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Key words: Exercise immunonutrition, nutritional supplements

In 2015 I and my co-editors (Louise Burke and Samantha Stear) published a book on Nutritional Supplements in Sport, Exercise and Health: An A-Z Guide. This contains contributions from more than 90 authors and deals with more than 140 topics. It is the culmination and update of a series of monthly publications which I initiated in the British Journal of Sports Medicine in 2009 and which ran until 2013. I launched this series because I was getting increasingly fed up with the way that some manufacturers (not all!) made a very great deal of money out of gullible and not-so-gullible athletes by selling them nutritional supplements which frequently were not very useful, were often poorly researched, if at all, and in some cases have actually had a deleterious effect on health.

The term dietary or nutritional supplement implies that it is something which supplements the diet. The Oxford English Dictionary definition of a supplement is "*Something added to supply a deficiency*". However, this definition is inconsistent with the majority of dietary supplement usage, with many supplements, or their individual ingredients, being nutrients or food chemicals for which the body does not have an estimated or theoretical requirement. Thus, there are clearly other factors that underpin their use by athletes.

Wherever possible we sought material from leading researchers in their field. If they were not able to write for us, then we approached people who were competent scientific writers and who had an interest in the topic under consideration. We were fortunate enough to obtain articles or opinions from researchers who are well known

in the fields of anti-doping, ethical principles and how to undertake good quality research.

In this talk I will be dealing with just a few, selected supplements, most of which are well known for one reason or another, for example, ergogenic benefits, which was our main focus. However, in particular, I will look at those supplements which have been reported to have a beneficial effect on the immune system. In addition, I shall highlight some aspects of the way in which future researchers might want to conduct studies in order to obtain the most accurate results, always bearing in mind the principle “Only if you are careful to handle all your samples in the same way, can you then make valid comparisons.”

MOBILIZING T-CELLS WITH EXERCISE FOR ADOPTIVE TRANSFER IMMUNOTHERAPY

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Key words: Hematopoietic stem cell transplantation, Viral infections, beta-2 adrenergic receptor, Virus-specific T-cells, T-cell mobilization

Hematopoietic stem cell transplantation (HSCT) is the preferred treatment for a wide range of hematological cancers and genetic disorders. While HSCT is a potentially curative treatment, viral infections and disease relapse are still common, accounting for ~78% of all deaths in the post transplant period. The conditioning regimen that is required to remove the underlying malignancy also eradicates the patient’s immune system. As such, widespread latent herpesviruses including cytomegalovirus (CMV) and Epstein-Barr virus, as well as non-latent community viruses such as adenovirus (AdV), influenza and respiratory syncytial virus, can result in significant levels of

morbidity and mortality in both adult and pediatric patients in the post transplant phase. The 21st century has seen adoptive T-cell transfer immunotherapy come of age, and many HSCT patients are now receiving donor-derived T-cell products to help prevent and control viral infections and disease relapse. Allogeneic (donor to patient) adoptive T-cell immunotherapy involves the extraction of antigen-specific T-cells from the peripheral blood of a healthy donor for subsequent transfer to the HSCT patient. The T-cells are transferred either immediately or after a period of *ex vivo* expansion that is designed to increase the number and purity of antigen-specific T-cells prior to transfer. The transferred T-cells are then able to proliferate and persist in the new host (sometimes for more than a decade after transplant) and have been shown through many clinical trials to effectively and safely prevent and treat post-transplant viral infections and virus-associated malignancies in a large number of patients.

Unfortunately, the logistical constraints associated with using donor-derived T-cells for transplant eliminates adoptive T-cell therapy as a treatment option for a large portion of HSCT patients. The 'direct isolation' method used to extract virus reactive T-cells from donor blood for immediate adoptive transfer is swift (1-2 days processing) but limited by the very low numbers of virus-reactive T-cells in the peripheral circulation (<1% of all lymphocytes). As such, very large and impractical volumes of blood are required to isolate enough virus reactive T-cells and, even then, the extracted cells still have to undergo a period of '*ex vivo* expansion' using cell culture techniques to generate sufficient numbers of antigen-specific T-cells for the transfer to be clinically effective. This expansion process can sometimes take several weeks depending on the antigen-specificity requirements of the T-cell therapeutic, causing critical delays in the delivery of the T-cell product. Some of these methods are also complex (i.e. involving gene transfer, clinical grade vectors or live virus) and costly. Although new 'rapid manufacturing protocols' can help increase the numbers of donor-derived viral-specific T-cells through *ex vivo* expansion in just 10-14 days, this is still too long for some patients and the numbers generated are not consistently large enough to be clinically effective after transfer. Moreover, the adoptive transfer of T-cells recognizing cancer antigens is considered a highly promising method for the prevention and treatment of disease relapse after HSCT, but translating this work into effective, clinically applicable treatments has been challenging, largely due to the

difficulties in manufacturing enough tumor reactive T-cells from healthy donors. Thus, identifying new methods to increase the yield of virus and tumor-reactive reactive T-cells from donor blood using both 'direct isolation' (1-2 days processing) and 'rapid manufacturing' (10-14 days processing) techniques is critical to increase the availability of adoptive T-cell therapy to a larger proportion of HSCT patients.

We have purported that the leukocytosis evoked by a single bout of dynamic exercise might augment our access to highly specialized and functional cell types from the peripheral blood compartment of healthy donors that would otherwise not be readily available under resting conditions. Our laboratory has focused on the potential adjuvant effects of exercise for mobilizing and expanding antigen-specific T-cells for adoptive transfer immunotherapy. We have shown that a single exercise bout mobilizes CD4+ and CD8+ T-cells specific to a wide range of latent herpesvirus antigens (including those derived from CMV, EBV and AdV) to the bloodstream of healthy donors. Although this mobilization is transient, it has allowed us to detect and isolate up to 5-times more virus-specific T-cells from a fixed volume of donor blood after exercise. We have also found that when T-cells are extracted from blood after exercise, they respond more readily to peptide stimulation and this has allowed us to manufacture many more virus and tumor-antigen specific T-cells from donor blood after exercise. Importantly, the T-cell products isolated and manufactured after exercise retain their ability to kill autologous target cells *in vitro* in both an antigen and MHC-restricted manner, indicating that they are likely to be effective *in vivo* following adoptive transfer. These findings indicate that exercise may serve as a simple and economical adjuvant to overcome some of the limitations associated with isolating and expanding sufficient numbers of antigen-specific T-cells from healthy donors for adoptive transfer. Our more recent work has shown that exercise augments the mobilization and 'priming' of antigen-specific T-cells by signaling through the β_2 adrenergic receptor, thus providing a potential target to augment the mobilization and *ex vivo* expansion of therapeutic T-cell products. Translating these findings to a clinical trial will ultimately determine if exercising healthy donors prior to/during blood collection will result in (i) a greater proportion of HSCT patients receiving allogeneic adoptive T-cell transfers to prevent/treat post transplant viral infections and disease relapse; (ii) larger T-cell numbers being transferred to the patient; (ii) shorter wait times for the patient to receive the T-cell product; and (iii)

improvements in clinical outcomes such as lower relapse rates and reduced incidence and severity of post-transplant viral infections. It is our hope that the successful 'bench to bedside' translation of these findings will result in single exercise bouts being used routinely in the clinic to augment the recovery and manufacture of donor-derived T-cell therapeutics.

EFFECTS OF LIFELONG TRAINING ON T LYMPHOCYTES SENESCENCE

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Key words: immunosenescence, masters athletes, inflammation

Aging has profound impact on the immune system, mainly on T-cells. The characteristics of immunosenescence from T cell pool, include poor vaccination responses and an inverted CD4:CD8 ratio, low numbers and proportions of naive T-cells (that would impair the capacity of the immune system to deal with new pathogens), larger numbers of effector memory T-cells in late stage of differentiation. Also, persistent infections, such as cytomegalovirus (CMV), would further reduce the naïve T-lymphocyte repertoire and drive effector T- cells into senescence (1). These senescent T-cells are apoptose resistant, incapable of dividing and thought to be the major cause of the chronic low-grade inflammation seen with age (2). Older persons with more pronounced chronic low-grade inflammatory profile are more prone to frailty and mortality (3). Furthermore, age-related loss of Treg function would contribute to a greater risk of autoimmune disease while the age-related increase in Treg numbers could result in compromised immune responses, increasing the risk of malignancies and infections. A recent model proposed that regular bouts of exercise can trigger preventive and/or restorative mechanisms of T-cell immunosenescence by inducing the apoptosis of senescent and functionally exhausted late stage differentiated T-cells and thus preventing overcrowding of the immune space (4, 5). Briefly, a 3 stage process is proposed: firstly, T-cells in a late differentiated stage are mobilized into the peripheral blood during exercise; Then, these cells leave the bloodstream to peripheral and/or inflamed tissues 1-2 h after exercise and a portion

of these senescent T cells subsequently undergo apoptosis, thus creating vacant space; Consequently, lowered T-cell numbers drive the positive feedback loop, increasing naive T-cell output, filling the vacant space and contributing to an expanded naive T-cell repertoire. Repetitions of this process in response to exercise would reduce the frequency of senescent T cells over time, lowering infection risk and increasing healthy longevity. Master athletes represent an interesting sub-demographic group to test this theory since they maintain a high training load and frequency throughout life, and represent an “exceptionally successful aging” process. The aim of this study was to evaluate the effects of lifelong training on senescent T lymphocytes and their response to acute exercise.

Material and Methods: Nineteen master athletes (53.5 ± 8.94 yrs.) who regularly participated in training and competitions for more than 20 years and a control group of 9 healthy individuals (53.7 ± 6.04 yrs.) participated in this study. All subjects performed a progressive test to exhaustion on a cycle ergometer. Blood samples were obtained before (Pre), 10 min after the test (Post) and 1 h after the test (1h). Phenotypic study of peripheral blood T-cells was performed by flow cytometry. Expression of genes of interest was done on T-cells purified by cell sorting. Group comparisons were assessed using the Mann–Whitney *U* test. Alpha level was set at 0.05. For the analyses of change, accounting for the multilevel design of the study [level 1 units (intra-individual) within each level 2 unit (individuals of different groups)], hierarchical random effects models (REM) were constructed using a multilevel modeling approach. **Results:** VO_{2max} was higher for master athletes when compared to the control group (P<0.001). No differences were founded for $CD4^+$ and $CD8^+$ T-cells and their subsets between master athletes and the control group at all times of measurement. Also, total $CD3^+$, $CD4^+$ and $CD8^+$ T-cells percentages did not increase with exercise. There were no significant differences in the proportion of Tregs either within the total lymphocyte population or within the CD4 T-cell population, between the two groups at baseline. There was no significant effect of acute exercise on the proportion (%) of Tregs within total lymphocytes and $CD4^+$ T-cells. However, acute exercise induced a significant increase in the number of Tregs at Post and returned to pre-exercise values at 1 h post for both groups. FoxP3, TGF-β and IL-10 mRNA expression was similar for both groups. For FoxP3 and TGF-β after exercise the number of detected cases was different between groups, with

higher results for master athletes (P < 0.05). IL-10 mRNA expression remained unchanged at all times of measurement for masters (Pre = 61.1%; Post = 66.7% and 1 h Post = 50% of all subjects), while in the control group there was a tendency for fewer cases expressing mRNA for IL-10 (Pre = 22.2%; Post = 55.6% and 1 h = 22.2%). Senescent $CD4^+$ and $CD8^+$ T-cells were higher in the control group when compared to masters before and 1 h after exercise. At baseline, masters had significant less percentage of senescent T lymphocytes (-6.7829±3.06%), $CD4^+$ T-cells (-5.8145±2.42) and $CD4^+$ senescent naive (-5.3182±2.5761) and effector memory (-4.3505±1.93%) T-cells. Regarding the $CD8^+$ T-cells, masters had significant less senescent $CD8^+$ T-cells (-13.0661±4.95), senescent T $CD8^+$ naive (-9.3624±2.09), central memory (-7.0282±3.065) and effector memory (-12.0034±5.49) cells. No significant effect of sports participation (controls *vs* masters) was noted for the % of senescent CD45RA expressing effector memory cells (EMRA) $CD4^+$ and $CD8^+$ T-cells. Senescent $CD4^+$ T-cells were mobilized by exercise only in the masters and returned to Pre-values in 1h. Senescent $CD8^+$ T-cells, CM and EM $CD8^+$ T-cells were also mobilized by exercise in the masters. These values return to Pre-values in 1h after the end of the protocol. In the control group, only the senescent $CD8^+$ CM T-cells increased at Post and their values remained elevated 1h after the test. The senescent EMRA $CD8^+$ T-cells did not increase at Post but decreased in 1h to values below those observed at Pre and Post, in the masters. Age had a negative effect on the naive $CD8^+$ T-cells. VO_{2max} associated negatively with the percentage of total lymphocytes and positively with the proportion of naive $CD4^+$ T-cells. The mRNA expression of the CCR7 gene for naive $CD8^+$ T-cells and the Fas-L gene for effector-terminal $CD8^+$ T-cells was not different between masters and controls and did not change in response to the maximal protocol test.

Conclusion: Master athletes have elevated anti-inflammatory markers and maintain the number and markers of activation of regulatory T cells as adaptive responses to exercise. Lifelong training decreased the percentage of senescent naive, CM and EM $CD8^+$ T-cells and senescent naive and CM $CD4^+$ T-cells. In both $CD4^+$ and $CD8^+$ T-cell subsets, the percentage of senescent EMRA T cells was also lower in the master athletes. Maintaining high levels of aerobic fitness during the natural course of aging may help prevent the accumulation of senescent T-cells and the maintenance of function and number of T regs, hallmarks of a younger immune system.

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EARLY LIFE EXERCISE PROMOTES FAVORABLE CHANGES IN GUT MICROBIAL ECOLOGY, PERSISTENT STRESS ROBUSTNESS, AND METABOLIC HEALTH”

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Key words: Gut-Microbial-Brain Axis, Stress Robustness, Fecal Metabolites, Prebiotic diets, Early life exercise

Regular physical activity positively impacts mental and physical health. The benefits of physical activity are often revealed in the face of challenge, including mental/physical stressors. Evidence suggests that physical activity status is an important determinant of stress robustness. Organisms that are stress robust can endure more intense and prolonged stressors before suffering negative health consequences; and they recover more quickly from those challenges. To better understand the mechanisms of stress robustness using a preclinical model, we varied physical activity status by housing juvenile or adult rats (inbred and outbred strains) with access to either a mobile or locked running wheel in their home cages. After 3-6 weeks, rats housed with mobile running wheels display physical changes

indicative of improved fitness, including increased endurance when tested on the treadmill, reduced abdominal adiposity when fed a high fat diet, increased lean body mass, changes in muscle citrate synthase etc. Most importantly for our work, however, is that physically active compared to sedentary rats have reduced adipose inflammation, no antibody suppression, no anxiety-like or depressive-like behaviors, and faster diurnal rhythm and sleep disturbance recovery, after exposure to an acute intense stressor (100, 1.5mA, 5-s tailshocks). Using this paradigm, we exploited the differences in stress robustness to reveal unique adaptations in stress responsive neurocircuitry that were necessary and sufficient for specific outcomes, including adaptations in serotonergic dorsal raphe neuronal responses responsible for anxiety-like and depressive like behaviors, and central sympathetic drive associated with immunomodulation. Our current work extends our assessment of adaptations produced by exercise to include commensal intestinal microbes (gut microbiota). The gut microbiota contributes to many aspects of host physiology. Changes in the gut microbiota early in development, for example, can impact host metabolism, immune function, and behavior that persist across the lifespan. In addition, the developing microbial ecosystem is more sensitive to change. We will present new evidence that physical activity 1) changes the gut microbial structure favoring a lean-promoting composition; 2) increases the abundance of beneficial microbial species; 3) increases butyrate-producing bacteria and butyrate, a short chain fatty acid implicated in metabolism and epigenetic processes. These effects are greater when running is initiated in adolescence compared to adulthood. Thus, early life presents a window of opportunity for producing adaptive changes in microbial composition that may contribute to some of the enduring positive impacts of exercise on mental and physical health.

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THE EFFECTS OF EXERCISE TRAINING ON KYNURENINES, METABOLISM, AND MENTAL HEALTH.

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Keywords: Skeletal Muscle, PGC-1alpha, coactivators, isoforms, exercise, depression.

Skeletal muscle condition and physical exercise play a clear role in the prevention and treatment of several diseases such as diabetes, obesity, sarcopenia (age-related loss of muscle mass and strength), and even neurodegenerative diseases and cancer. Skeletal muscle is an extremely plastic tissue that can use energy to generate work, generate energy by breaking down proteins into amino acids, undergo atrophy, hypertrophy, and even change its metabolism when stimulated by distinct challenges (i.e. endurance versus resistance training). Accordingly, different exercise programs can be used to ameliorate different conditions. Endurance training increases muscle energy efficiency, oxidative capacity, resistance to fatigue as well as cardiovascular function, whereas resistance training leads to muscle hypertrophy and can be used to treat sarcopenia.

Although our understanding of the mechanisms that regulate skeletal muscle adaptation to different exercise challenges is still incomplete, proteins of the peroxisome proliferator-activated receptor-gamma coactivator-1alpha (PGC-1alpha) family of transcriptional coactivators have been shown to play important roles in these processes. PGC-1alpha coactivators are expressed in energy-demanding tissues like fat, muscle, liver and brain. Interestingly, one single gene can be differently regulated by alternative promoter usage and alternative splicing to generate discrete PGC-1alpha variants with different biological activities. PGC-1alpha1 (the founding member of the family) is activated by aerobic exercise and regulates genes involved in mitochondrial biogenesis, adaptive thermogenesis, lipid

and glucose homeostasis, fiber-type switching, among other. For these reasons, deficiencies in PGC-1alpha1 activity have been suggested to be involved in pathogenic conditions such as obesity, diabetes, sarcopenia, and neurodegeneration. Conversely, it has been shown that overexpression of PGC-1alpha1 in murine skeletal muscle has several beneficial effects. PGC-1alpha4 is induced by resistance exercise training and specifically promotes skeletal muscle growth and strength. Importantly, transgenic animals with elevated PGC-1alpha4 levels in skeletal muscle show increased exercise performance, and resistance to atrophy and to cancer-induced cachexia.

Until recent years, changing skeletal muscle mass and condition through diverse exercise interventions was seen as a way to improve systemic bioenergetics and metabolic disease. Although this is indeed an efficient strategy to fight diseases such as obesity and diabetes, it is increasingly appreciated that skeletal muscle function can impact systemic physiology by changing the nature and quantity of circulating factors (myokines). These include molecules involved in angiogenesis (VEGF-A), cellular hypertrophy (Myostatin and IGF1), immune cell recruitment (IL6, 8, and 15), adipocyte-mediated thermogenesis (FGF21, meteorin-like, myostatin, Fndc5), and neuroinflammation (kynurenine), among other.

Of particular interest are the well-known effects of physical exercise on mood, behavior, and cognition. Indeed, physical exercise has often been described as the most underutilized treatment in psychiatric disease. However, the mechanisms that mediate its therapeutic effects are largely unknown. We have recently identified a novel biochemical pathway, activated in exercised muscle, that changes tryptophan-kynurenine metabolism and protects from stress-induced depression. This results from the increased conversion of the tryptophan metabolite kynurenine (KYN) into kynurenic acid (KYNA) in skeletal muscle. Reducing kynurenine levels protects the brain from neuroinflammation and other changes associated with depression, anxiety, and schizophrenia, among other diseases. The master regulator of this detoxification pathway is the transcriptional regulator PGC-1alpha1, which is itself activated by exercise and mediates many of the effects of exercise training. Muscle PGC-1alpha1 induces the expression of several kynurenine aminotransferases (KATs), which convert KYN to KYNA thus protecting the brain from insults known to be associated with psychiatric disease.

Understanding the molecular mechanisms that regulate how skeletal muscle adapts to different stimuli, and how these pathways can be targeted to harvest some of the beneficial effects of physical exercise can open important therapeutic opportunities.

ORAL PRESENTATIONS

LOST IN TRANSLATION – GETTING YOUR RESEARCH MESSAGE ACROSS

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Often the immunology research process sees its end at the acceptance of a research article for publication and authors sometimes overlook the notion that the most important outcomes are dissemination and implementation of findings. The priority should be answering relevant questions that affect real people in a given clinical, sporting or community context. Research outcomes from cellular, biochemical and molecular immunology studies are crucial for developing guidelines for healthy lifestyle habits and exercise routines, contemporary practices, and policies in immunology. However, these applications can only be realised if the research process is shared, and results contextualised and translated for specific cohorts and populations.

Timely discussion and dissemination of research outcomes requires effective strategies and appropriate technical and meaningful language for different audiences via traditional scientific publication, conference proceedings and social media strategies. Research communication strategies should span scientific, medical and allied health disciplines, local, national and international contexts and translate into non-scientific communities. Researchers need to identify, develop and implement

new ways of putting highly scientific information and outcomes into context using real world examples. For example, our research group has developed a model for using salivary immunoglobulin A as a marker of the risk of upper respiratory tract infection. This work has involved laboratory and field research, clinical evaluations, and development of education materials for athletes, coaches and clinicians. However, the application of this knowledge has been variable and often inappropriately applied world-wide, i.e. the transferability of results obtained from highly trained athletes might not apply directly to the wider population, and vice versa.

Although researchers are mostly judged on publications and research income, research teams should commit to the social, community and clinical responsibility in their chosen field of study and the impact of their research evidence in guiding clinical and sport training practices. Funding agencies now expect real world applications and a substantial practical return on the investment by stakeholders, participants and researchers. We will present a continuum for translating research evidence into practical applications.

Key words: Dissemination, application, immunology.

IMMUNE CELL PROFILES DISTINGUISH AUSTRALIAN OLYMPIC ATHLETES WITH OR WITHOUT UPPER RESPIRATORY SYMPTOMS

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Introduction Preventing upper respiratory symptoms (URS) during training and competition, is recognized as critical to optimum athletic performance. While exercise has both acute and chronic effects on the immune system, few parameters are associated with URS prevalence. The rapid growth in high throughput analysis is now allowing a more detailed examination of the immune system. Mass cytometry is a novel high resolution method that allows the simultaneous assessment of >40 cell populations from a single sample with sensitivity to detect rare cell populations below 10^{-4}. We examined differences in immune cell profiles between athletes selected for the Rio 2016 Olympics who experienced URS in the lead up to the games and those with good health.

Methods A cross-sectional study compared peripheral immune cell frequency in 75 elite Australian athletes. URS prone athletes were classified based on responses from a retrospective illness symptoms log for the previous month. Peripheral blood immune cell frequency of T cells subsets, B cell subsets, monocytes, natural killer and dendritic cells was assessed via mass cytometry (Helios, Fluidigm). Mass cytometry data was normalised and immune cell profiles were compared between groups. Immune cell gene expression was assessed using the Immune Profiling Panel (NanoString Technologies).

Results The illness symptoms log determined two groups; URS prone athletes (n=39; age: 25±4.2; mean±SD) and healthy athletes (n=36, age: 24.2±3.6; mean±SD). URS prone athletes had a significantly higher frequency immune cells (p=0.014), including T cells (p=0.022), CD4+ T cells (p=0.012) CD4+ memory T cells (p=0.013) and CD4+ naive T cells (p=0.036), CD8+ memory T cells (p=0.22), B cells (p=0.041) and plasma cells (p=0.037). Immune gene expression signatures further differentiated immune cell frequencies between groups.

Discussion Regular intense exercise can exert a chronic effect on the immune system that may influence URS prevalence in some athletes. The observed differences in immune cell profiles yield insights into immune regulation. These data support the value of new technologies including mass cytometry and digital gene expression analysis in profiling immune phenotypes at greater resolution than has been possible previously. The utility of these approaches in illness prediction needs to be further evaluated in prospective studies.

MULTIDIMENSIONAL ANALYSIS REVEALS INCREASING PHENOTYPIC CHANGES IN THE TOTAL NEUTROPHIL COMPARTMENT DURING 8 CONSECUTIVE DAYS OF ENDURANCE EXERCISE

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Intensified endurance exercise is associated with increased risk of upper respiratory tract infections (URTI) likely caused by an impaired immune response (Nieman 2000). Peripheral blood neutrophil counts increase upon exercise and recover within 6-24 hours, this accounts both for anaerobic as well as aerobic exercise bouts (Robson et al. 1999). We have previously described the mobilization of 3 neutrophil subsets with different functional characteristics in response to acute inflammation such as evoked by systemic LPS challenge in healthy volunteers. These cells can be identified by differential expression of FcgammaRIII (CD16) and of L-selectin (CD62L) (Pillay et al. 2012).This study tested the hypothesis that intensified endurance exercise leads to impaired recovery of the innate immune response characterized by differential mobilization of neutrophil subsets normally absent in the peripheral blood.

The kinetics of the innate immune response were studied in 30 healthy amateur cyclists (11 female, 19 male) participating in an 8-day strenuous cycling tour (mean daily distance of 160 km and 2300 altimeters). The innate immune response was studied by analysis of peripheral blood neutrophils both in terms of absolute numbers

as well as phenotype. Neutrophils were analyzed by flow cytometry with the use the multidimensional analysis method FLOOD (Jansen et al. 2016). The overnight recovery of the innate immune response was followed in the mornings of day 5 and day 8 and compared with the morning day 1 (baseline).

Repeated endurance exercise led to an increase in total neutrophil counts (1.26 fold-increase; 95%CI 1.01-1.51 p=0.0431) in the morning at day 8. Flow cytometry measurements revealed the appearance of 2 neutrophil subsets: $CD16^{bright}CD62L^{dim}$ and $CD16^{dim}CD62L^{bright}$. Deep phenotyping of flow cytometry data revealed a complex change in neutrophil phenotype, characterized by decreased expression of both CD11b and CD62L and marked increased expression of LAIR-1, VLA-4 and CBRM1/5. The changes in expression were found on all neutrophils present in the blood. Strikingly, in strong contrast to our findings during LPS challenge, these neutrophils did not upregulate classical degranulation markers. In fact, our FLOOD analysis revealed that the exercise induced neutrophil phenotype did not overlap with the neutrophils after LPS challenge.

In conclusion, a buildup in changes in the neutrophil compartment was identified in the blood at day 5 and 8 of endurance exercise with a complex change in marker expression. Differential functioning of these changed granulocytes may play a role in the increased risk for URTI during intensified training.

SUBMAXIMAL AEROBIC EXERCISE INDUCES MAIT CELL LYMPHOCYTOSIS BUT DOES NOT ALTER HOMING AND ACTIVATION MARKERS

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Mucosal associated invariant T (MAIT) cells occupy a unique niche, having properties of both the innate and adaptive immune systems (Godfrey, 2015). Identified by expression of the semi-invariant T cell receptor Vα7.2 and CD161, MAIT cells are an understudied population within exercise immunology with only minimal data indicating these cells are affected by exercise (Hanson, unpublished). These innate-like lymphocytes aggregate at the mucous membranes, however it is unknown if exercise alters their activation status or aids in their trafficking to the mucosa. **PURPOSE:** To determine circulating MAIT cell number and frequency along with activation (CD69 expression) and tissue homing marker (CCR4, CCR5, CCR6) expression before and after submaximal aerobic exercise. **METHODS:** 17 healthy young males [age 22 (4), VO_2max 51.6 (10.2) mL/kg/min, V_T 2.7 (0.6) L/min, % fat 18.0 (5.0%)] performed a graded exercise test on a cycle ergometer until volitional fatigue. Ventilatory threshold (V_T) was determined and on the next visit, participants cycled for 40 min at 90-98% of V_T following an overnight fast. Venous blood samples were obtained at rest, 0h and 1h after exercise. Peripheral blood mononuclear cells were isolated using density gradient centrifugation and were labelled to identify specific MAIT cell populations using flow cytometry. Data are expressed as mean (SD). **RESULTS:** $Vα7.2^+CD161^+$ MAIT cells were 3.1 (1.7%) of all T cells at rest and significantly increased to 4.0 (2.4%; P=0.005) at 0h. MAIT cell numbers increased by 68% following exercise [Rest: 40 (25) 0h: 67 (54 cell/mL); P=0.012] before returning to resting levels at 1h. $CCR5^+$ MAIT and $CD69^+$ MAIT cell numbers increased by

84% [Rest: 31 (26), 0h: 57 (58 cells/mL); P=0.018] and by 67% [Rest: 3 (1), 0h: 5 (1 cells/mL); P=0.05] with exercise, respectively. $CCR5^+$ expression [74.2 (34.1%); mean fluorescence intensity: 7367 (4977 a.u.)] and $CD69^+$ expression [12.1 (18.1%)] were all unchanged over time. **CONCLUSIONS:** MAIT cell numbers transiently increase after exercise, follow a biphasic response, and appear to be preferentially mobilized with T cell subsets. These findings support and extend our previous work; however, the magnitude of the submaximal response was attenuated relative to maximal exercise. MAIT cell numbers expressing activation and homing markers following exercise are higher but are driven by the exercise-stimulated lymphocytosis, rather than intrinsic cellular changes.

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Key words: MAIT cells, aerobic exercise, chemokines, activation

ENDOCRINE, IMMUNE AND INFLAMMATORY ADAPTATIONS IN MEN FOLLOWING EXERCISE-INDUCED CHRONIC STRESS

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Athletes elevate training load to improve physical performances. This process may lead to detrimental overreaching states (functional or non-functional) or to the more serious state, the overtraining syndrome (OTS). Overreaching is difficult to diagnose and recovery from these states may take weeks to years (Meeusen et al., 2013). Preliminary evidence suggests that blunted exercise-induced salivary testosterone and cortisol responses to a 30-min, high-intensity cycling bout may be indicative of overreaching (Hough et al., 2013). This test may not be useful for non-cyclists, therefore, a 30-min, high-intensity running bout ($RPE_{treadmill}$) using the Borg scale as a measure of exertion has been developed. Additionally, $RPE_{treadmill}$ induced reproducible plasma cortisol and testosterone responses in our laboratory (unpublished data). While overreached immunosuppression may occur (Lancaster et al., 2003). Cortisol influences inflammation regulation by elevating neutrophils and suppressing lymphocytes (Malm et al., 2004). Therefore, the reported blunted cortisol when in an overreached state may be linked with a suppressed immune function. Furthermore, incidence of upper respiratory tract infections increased with a 40% decrease in secretory immunoglobulin A (SIgA) after 5 days of military combat, returning to baseline levels after 1 week of recovery (Tiollier et al., 2005). This study aims to examine $RPE_{treadmill}$-induced leukocyte proliferation, neutrophil phagocytic activity, plasma cortisol and testosterone, SIgA and cytokine responses, before and after a 12-day intensified-training (intercalated a)90-min run at ~60% velocity at maximal oxygen uptake; b)5-km time-trial; c)70-min run at ~13 (somewhat hard) on the Borg scale) and 5-day recovery periods. To date, 4 (aim N = 8) healthy, active males (means ± SD; age: 24 ± 6 y; height: 175 ± 6 cm; body mass: 72.3 ± 6.2 kg; maximal oxygen uptake: 54 ± 6 $ml \cdot kg^{-1} \cdot min^{-1}$) completed the study. Recovery-stress and URTI questionnaires were completed before and after training and recovery. Flow cytometric analysis of leukocyte subsets and neutrophil phagocytic activity was performed. Inflammatory markers will be analyzed upon cessation of data collection (April 23rd). Blunted exercise-induced SIgA is expected following chronic stress. Training volume increased by ~178% during the 12-day period. Exercise-induced plasma cortisol and testosterone increased (~16%) and blunted (~15%) after training, respectively. Exercise-induced neutrophil phagocytic activity elevated by ~109% Pre-training and blunted by ~36% Post-training. Pre-training, $RPE_{treadmill}$ reduced total whole blood leukocytes whilst neutrophils elevated. Opposite responses were observed Post-training. This study may uncover some effects of overreaching/OTS in

immunity and inflammation and propose the utilization of the $RPE_{treadmill}$ as a novel, suitable tool to be used to highlight overreaching aiming to reduce OTS.

INFLAMMATION STATUS OF HEALTHY UNTRAINED YOUNG MEN: INITIAL RESPONSE TO RESISTANCE TRAINING

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Resistance training (RT) is recommended for the maintenance and improvement of health (Kraemer, Ratamess, & French, 2002). RT has been shown to reduce markers of subclinical inflammation (Calle & Fernandez, 2010) and reduce fat stores (Donnelly et al., 2009). Our primary aim was to study the effects of four-week resistance training (RT) period on inflammation markers in previously untrained men and the possible relationship between the changes in abdominal fat mass and the changes in inflammation status.

A total of 68 physically active and healthy untrained young men started with RT (3x8-15x50-80% of 1RM) performed twice a week for a 4 week. In addition, the control group (n=12) was asked to maintain their habitual physical activity and exercise level. Abdominal fat mass was estimated with dual-energy absorptiometry (DXA) and fasting venous blood samples were drawn from an antecubital vein before and after RT. High-sensitivity C-reactive protein (hs-CRP), interleukin (IL)-6, monocyte chemo attractant protein 1 (MCP-1) and selected adipocytokines (resistin, adiponectin and

leptin) were determined by enzyme-linked immunosorbent assay (ELISA) with commercial reagents.

RT significantly increased circulating resistin concentration ($p = 0.039$, ES = 0.546) and MCP-1 concentration ($p = 0.039$, ES = 0.548). However, a significant decrease in circulating leptin concentration was observed ($p = 0.006$, ES = 0.799). After the RT period, abdominal fat mass was significantly reduced (-3.2 ± 6.8 %, $p=0.001$, ES=0.969). Significant correlation was observed between change in abdominal fat mass and change in leptin concentration. All the variables stayed statistically unaltered in control group.

Already short-term 4 week RT reduced abdominal fat mass and circulating leptin concentration. In addition, to these health beneficial results, resistance training induced unwanted pro-inflammatory alterations. RT induced a significant increase in MCP-1 and resistin concentrations. Taken together, the results of this study indicate that the initial response to RT has anti-inflammatory effect but it may also elicit an increase in some of the pro-inflammatory markers in an untrained population. Thus, caution must be taken when designing resistance training programs for people with no background in RT.

Keywords: body composition, leptin, resistin, MCP-1, exercise training

ANAPHYLAXIS DURING PHYSICAL EXERCISE

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Keywords: Exercise-induced anaphylaxis. Wheat allergy. Omega-5 gliadin.

Background: Exercise-induced anaphylaxis is a rare disorder in which anaphylaxis occurs during or following physical activity, and presents with severe allergic reaction involving multiple systems (cutaneous, respiratory, gastrointestinal and/or cardiovascular). A distinct subtype is characterized by onset of symptoms of anaphylaxis only if physical activity occurs associated with a specific food allergen ingestion.

Clinical case: We describe a case of a 59-year-old man with two episodes of anaphylaxis that occurred during physical activity – walking, after dinner time. In both episodes he presented with rhinoconjunctivitis, urticaria, angioedema, dyspnea and loss of consciousness. The meal consisted of vegetable soup and wheat based bread. The episodes occurred following coronary heart surgery and after making lifestyle changes: light dinners consisting of soup and bread, regular exercise (mainly, walks after dinner) and prescribed medication (furosemide, atorvastatin and aspirin). Physical exercise as well as cereals ingestion alone was tolerated. There was no previous history of allergic disorders.

He was admitted in our Immunoallergology Department for further investigation. Total IgE was elevated (443 IU/mL). Skin prick tests to aeroallergens and cereals were negative. Prick-to-prick tests with bread flours were positive to wheat, rye, barley and corn (wheals diameter 8, 10, 4 and 4 mm, respectively). Specific IgE was positive to wheat (0,9 kU/L), rye (4,2 kU/L) and the molecular component ω-5-gliadin (9,7 kU/L).

These results strongly support the diagnosis of food dependent exercise-induced anaphylaxis (FDEIA). The foods most commonly implicated are wheat, shellfish, tomatoes, peanuts, and corn, though a wide variety of foods can be associated. A distinct subtype triggered by wheat ingestion is called wheat dependent exercise-induced anaphylaxis (WDEIA), which the major causative allergen is ω-5-gliadin. Exercise-induced anaphylaxis to food allergens focuses on two levels of cofactor modulation: exercise increases the bioavailability and influences the distribution of certain allergens, and decreases the threshold for activation of mast cells and basophils.

The patient was advised to avoid eating wheat and rye 3 hours before and 1 hour after exercising. Patient education included detailed information on foods that may contain hidden cereals and a written emergency plan including self-injectable adrenaline. The patient was advised to avoid other nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin was replaced by clopidogrel. In the last 3 years he continued to eat corn, barley, oats, and rice. With the avoidance measures taken, no more allergic symptoms or anaphylactic episodes occurred.

Conclusion: This case is an example of WDEIA where elicitation of anaphylaxis occurred in the presence of physical exercise and daily intake of aspirin.

Identifying both the trigger allergen and the dependence on cofactors is essential in allergologist's patient routine assessment, which help to avoid possibly life-threatening anaphylactic events in the future.

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DYSREGULATED NK-CELL FUNCTION DURING LONG-DURATION SPACEFLIGHT

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Before we can ethically send Astronauts to distant locations in space, such as Mars or asteroids, it is critical that we understand how spaceflight affects the human immune system. Previous post-flight studies suggest that immune functions, including NK-cell cytotoxicity, are dysregulated following spaceflight (Meshkov and Rykova, 1995; Konstantinova et al., 1993). These prior data are confounded, however, by the acute stress of high-G re-entry and acclimation to terrestrial gravity. For the first time, our lab has collected blood samples from Astronauts on the International Space Station (ISS) and comprehensively assessed the real-time effects of spaceflight on NK-cell cytotoxic activity (NKCA) and phenotype using flow cytometry. In this study, 8 Astronauts and 8 ground-based controls provided concomitant blood samples at 8 time points before, during, and after a 6-month ISS mission: 180 days before launch (L-180), L-60, Flight day (FD)-90, 1 day before return (R-1), day of return (R+0), R+18, R+33, and R+66. NKCA was measured against tumor cell lines of leukemic (K562), multiple myeloma (U266), and lymphoma origin (221.AEH and 721.221). Our flight study is the first to show that anti-tumor NKCA is inhibited during and after long-duration spaceflight. Astronauts had higher pre-flight NKCA than ground-based controls; however, NKCA decreased below controls during spaceflight (FD90) and immediately upon return (R+0) ($p<0.05$). Furthermore, first-time flyers had decreased NKCA relative to ground-based controls and repeat flyers at multiple points during and after spaceflight (FD90, R+0, R+18,

and R+33) ($p<0.05$). There was no effect of spaceflight on NK-cell phenotype (i.e. expression of activating and inhibitory receptors), NK-cell conjugation with target cells, or expression and degranulation of perforin and granzyme b in response to target cells ($p>0.05$). Impaired NK-cell cytotoxicity is of grave concern for future space travelers as decreased NK-cell function is associated with increased risk of cancer, especially skin and blood cancer (e.g. leukemia, multiple myeloma, and lymphoma) (Vineretsky et al., 2016). Radiation levels are very high in space, particularly outside of low Earth orbit, and skin and bone marrow (source of blood cancer cells) are particularly sensitive to radiation-induced tumorigenesis (Barcellos-Hoff et al., 2005). The combination of impaired NK-cell function and prolonged exposure to cosmic radiation during a 3-year Mars journey is a recipe for cancer. Future studies should determine the mechanisms underpinning this impaired NK-cell function during spaceflight, so that countermeasures can be developed to maintain immunity during long-duration missions, especially for first-time flyers.

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THE IMPACT OF A 6-MONTH MISSION TO THE INTERNATIONAL SPACE STATION (ISS) ON SALIVARY ANTIMICROBIAL PROTEINS

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Maintaining immune system integrity is of paramount importance for astronauts embarking on long-duration spaceflight missions. Immune system dysregulation has been documented during and after short-duration (14-days) spaceflight missions (Mehta et al., 2014), although less is known about the potential impact missions of longer duration will have on host immunity (Crucian et al., 2008). Salivary antimicrobial proteins (sAMPs), such as lactoferin and lysozyme, act as a first line innate host immune defense (Fabian et al., 2012). We determined the impact of a 6-month mission to the International Space Station on a host of salivary biomarkers in both ISS crewmembers (n=8) and ground-based controls (n=7). All participants provided 7-consecutive days of saliva samples immediately after waking at various time points over a ~14-month period; pre-flight (L-180/L-60), in-flight (FD10/FD90/R-1) and post-flight (R+0/R+18/R+33/R+66). Saliva samples collected over the 7-days were pooled and analyzed for: C-reactive protein (CRP), salivary IgA, lysozyme and lactoferrin. Lysozyme levels were significantly elevated in crewmembers when compared to controls (p=0.009) at FD10 (33.3 x 10^3 vs. 8.1x 10^3 ng/mL, p = 0.014) and FD90 (31.0 x 10^3 vs. 6.0 x 10^3ng/mL, p = 0.015). Lactoferrin levels were also significantly elevated in crewmembers when compared to controls (p = 0.001), at FD10 (65.6 x 10^5 vs. 20.4 x10^5 pg/mL, p = 0.043). No significant differences were observed for CRP or salivary IgA between crewmembers or controls over the duration of the study (p > 0.05). In conclusion, salivary lactoferrin and lysozyme concentration increases during long duration space flight, which may be due to

sustained elevations in sympathetic nervous system activity. Whether or not these have clinical implications for crewmembers embarking on exploration class missions (i.e. to Mars or an asteroid) remains to be determined.

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CAN CARBOHYDRATE AND PROTEIN INTAKE PREVENT GUT-IMMUNE PERTURBATIONS INDUCED BY EXERTIONAL-HEAT STRESS?

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Physical exertion in hot ambient conditions perturbs the integrity of the

gastrointestinal tract leading to endotoxaemia and subsequent systemic cytokine responses. Such perturbations have been linked to gastrointestinal symptoms and adverse health and performance implications. To date, it is unknown whether nutrient intake, which is a common-practice during prolonged exercise, can attenuate gastrointestinal perturbations induced by exertional-heat stress (EHS). The study, therefore, aimed to determine the effects of carbohydrate and protein intake during EHS on intestinal injury, permeability and inflammation, gastrointestinal symptoms, systemic endotoxin and cytokine responses. Using a randomised repeated-measures design with one week washout, eleven endurance runners completed 2 h running at 60% VO2max in 35°C (27% relative humidity) consuming either 15g glucose (6% w/v) (GLUC), energy-matched whey protein hydrolysate (WHEY), or water (WATER) before and every 20 min during exercise. Rectal temperature and gastrointestinal symptoms were recorded every 10 min during exercise. Blood samples were collected pre- and post-exercise, and during recovery to determine plasma intestinal fatty-acid binding protein (I-FABP), cortisol, endotoxin, and cytokine concentrations. Pre- and post-exercise faecal samples were collected to determine calprotectin. Urinary lactulose:rhamnose was used to measure small intestinal permeability. GLUC and WHEY abolished the post-exercise increase in I-FABP (trial*time, $p<0.001$) and reduced small intestinal permeability compared to WATER (trial effect, $p=0.002$); with WHEY reducing small intestinal permeability more than GLUC ($p<0.05$). Total- and upper-gastrointestinal symptoms were greater with WHEY, compared to GLUC and WATER ($p<0.05$). Endotoxaemia was observed post-exercise (10.2pg/ml; time effect, $p=0.001$), with no difference between trials. However, post-exercise anti-endotoxin antibodies were higher on GLUC ($p<0.01$) and WHEY ($p<0.05$) compared to WATER, indicating improved endotoxin clearance capacity with nutrient intake. Plasma IL-6 and cortisol concentrations increased post-WATER, and were higher than GLUC, but not WHEY (trial*time, $p=0.048$ and $p<0.001$, respectively). Plasma IL-8, IL-10 and IL-1ra concentrations increased post-exercise on all trials (time effect, $p<0.01$). No differences were observed pre- to post-exercise or between trials for plasma IL-1â, TNF-a and faecal calprotectin concentrations. Anti-endotoxin antibodies were negatively associated with I-FABP, permeability and inflammatory cytokines ($p<0.05$). In conclusion, carbohydrate (i.e., glucose) and protein (i.e., whey) intake during EHS reduces intestinal injury and small intestinal permeability, supports endotoxin clearance and improves

inflammatory cytokine profiles. However, protein appears to contribute to the development of gastrointestinal symptoms, making carbohydrate a more appropriate recommendation for supporting gut-immune health during EHS.

DIFFERENCES IN THE NASAL NEUTROPHIL COUNT BETWEEN MARATHONERS PRESENTING OR NOT EXERCISE-INDUCED BRONCHOCONSTRICTION

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Keywords: Exercise-induced bronchoconstriction; marathon runners; nasal mucosa; upper-airway.

Introduction: Exercise-induced bronchoconstriction (EIB) is defined as a transient narrowing of the airways that occurs after exercise1. The objective of this study was to compare differential cell count in the upper airway, nasal mucosa, of marathon runners with and without EIB. Methods: Thirty-eight male amateur marathon runners were recruited from the International Marathon of São Paulo, 2012. The study was approved by the ethics committee on human research of the Federal University of São Paulo under number 0573/11. All participants underwent pulmonary function testing, cardiopulmonary test and a nasal swab was performed to obtain the differential cell count in cytogram of nasal mucosa. Results: Twenty-nine athletes

showed normal results in pulmonary function test and 9 subjects presented a decrease higher than 10% in expiratory forced volume in first second, characterizing an EIB diagnosis. The differential count of cells in nasal mucosa performed by cytogram analysis did not presented differences in Δ distribution between groups for epithelial cells (p=0.47), lymphocyte (p=0.15) and eosinophil (p=1). On the other hand, neutrophils showed a significantly difference (p=0.02) between groups. Discussion: The neutrophil count in EIB athletes group is significantly higher. Taking into account that the chemokine IL-8 concentration is elevated in both groups after marathon race2and that IL-8 is an important chemotactic factor, probably the response to IL-8 is different between groups. The difference could be related to expression of IL-8 receptor or due to IL-8 protein polymorphism, as is demonstrated in the literature. In addition, previous studies showed that the airway it's a continuous, so the upper airway could mirror the conditions of lower airway through a less invasive method than induced sputum, using the nasal cytogram3,4. Conclusion: The utilization of a minimal invasive method in this study showed that it's possible to analyze the inflammation of airway and that athletes with EIB present an expressive elevation of neutrophil infiltrate when compared with non EIB athletes. The difference in neutrophils count in nasal mucosa, can be due to different responses to the IL-8 chemokine.

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EFFECTS OF THERAPEUTIC EXERCISE TRAINING ON SYSTEMIC INFLAMMATION IN SMOKE EXPOSED MICE

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Introduction: Long-term cigarette smoking has an important extrapulmonary toxicity. Recent studies suggested that inflammatory processes in the pulmonary systems spill over to systemic inflammation which negatively affects several extrapulmonary organs and tissues. Regular exercise training has been shown to be an effective non-pharmacological treatment strategy which has anti-inflammatory properties. The aim of the study was to investigate the effects of regular exercise training systemic inflammation in long term smoke exposed mice.

Methods: C57bl/6j-mice (n=30) were randomly separated into three groups to receive either: (1) 8 months exposed to mainstream cigarette smoke for 6 h/day, 5 days/wk (smoke-exposed (SE) group), (2) 8 months cigarette smoke and 2 months of exercise training for 30 min/day, 5 days/wk (SEex group) and (3) age matched controls with no specific treatment (Con group). Inflammatory markers and adhesion molecules on lymphocytes were analyzed by flow cytometry (Beckman Coulter, EPCIS XL). Levels of various inflammatory plasma cytokines were quantified by a multiplexed fluorescent bead-based immunoassay (Luminex; Myriad RBM, Austin, TX).

Results: Mice of the SE group showed a significant decline of VO_{2max} and V_{max}, which was reversed by exercise training ($p<0.05$). The increased expression of

VCAM-1, ICAM-1 and CD62L on $CD3^+$, $CD3^+CD4^+$ and $CD3^+CD8^+$ cells after smoke exposure was significantly down-regulated in the SEex group ($p<0.05$). Similarly, several plasma cytokines such as interleukin-1alpha (Il-1alpha), monocyte chemotactic protein-3 (MCP-3), macrophage inflammatory protein-1beta (MIP1beta), MIP-1alpha, Factor VII, Tissue inhibitors of metalloproteinases-1 (TIMP-1), and CD40L, which were increased in SE mice, were down-regulated by therapeutic exercise training.
Conclusion: Exercise training reversed cigarette smoke-induced systemic inflammation and inflammatory priming of lymphoyctes. It is assumed that the systemic anti-inflammatory effects of exercise are beneficial to several extrapulmonary impairments after smoke exposure.

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ASSOCIATIONS BETWEEN METABOLIC AND INFLAMMATORY CHANGES IN OBESE MIDDLE-AGE MEN AFTER 24 WEEKS OF COMBINED TRAINING

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Obesity increases the circulating levels of pro-inflammatory markers, and the incidence of non-communicable diseases (NCDs). In contrast, physical exercises may have a major role in modulating levels of pro and anti-inflammatory markers deregulated by an excess of adipose tissue. In a previous study, we concluded that 24 wk of combined training (CT) in obese men were effective to reduce pro-inflammatory markers, and provided an anti-inflammatory effect on metabolism (BRUNELLI et al. 2015). In another study (in press), we observed a different

metabolic profile between obese men that performed or not 24 weeks of CT, suggesting new metabolites candidate biomarkers. Thus, the aim of this study was to associate the changes (%Δ) in inflammatory markers and metabolites, after 24 weeks of CT. Twenty-two obese middle-aged men (48.2 ± 6.1 years; Body Mass Index 31 ± 1.4 kg/m²) participated in the study. The CT was performed with moderate-to-high-intensity, three times a week (resistance and aerobic training in the same session) during 24 weeks. The pro and anti-inflammatory markers (TNF-α, CRP, IL-6, IL- 10, IL-15, resistin, leptin, and adiponectin) measurements were determined by enzyme-linked immunosorbent assay (ELISA). The metabolites were identified by 1H NMR-based metabolomics. A PLS-DA model was conducted with fold change values (post/pre). Twenty metabolites with higher VIP score were selected as the most significant in the segregation of groups (tyrosine, 2-oxoisocaproate, histidine, pyruvate, phenylalanine, isoleucine, choline, betaine, carnitine, lysine, glucose, creatinine, ornithine, valine, alanine, leucine, glutamine, asparagine, 2-aminobutyrate, and lactate). Pearson's or Spearman correlations coefficients were used to associations between metabolites and inflammatory markers changes (%Δ). The software used was Prism GraphPad 5.0. The significance criterion adopted was 5% ($p<0.05$). There was a negative correlation between adiponectin, 2-aminobutyrate (r= -0,750) and pyruvate (r= -0,641); IL-6, alanine (r= -0,618) and lysine (r= -0,666); leptin and glutamine (r= -0,782). Positive correlations were also observed between IL-6 and isoleucine (r= 0,600); IL-10 and glutamine (r= 0,866); CRP, glucose (r = 809) and ornithine (r= 724) were showed. These results showed that the changes in the metabolic profile, induced by 24 weeks of CT, in the metabolism of obese men are related to concomitant changes in the inflammatory profile.

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Keywords: Metabolomics, inflammatory markers, obesity, physical exercise, metabolism

.MULTIFACTORIAL CARDIOVASCULAR RISK INTERVENTION IN AN EARLY STAGE OF TYPE 2 DIABETES IN OLDER ADULTS: THE EFFECT OF EXERCISE TRAINING AND METFORMIN

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Introduction: The management of diabetes in elderly is a complex process due to the increased prevalence of comorbidities, heterogeneous functional status, and geriatric syndromes(Bell & Saraf 2016), and although glucose regulation plays a central role on the standards of medical care, greater reductions on other cardiovascular risk factors, especially hypertension and lipid profile, may be the key factor to decrease morbidity and mortality (American Diabetes Association 2016). Nevertheless, the relative clinical value of exercise training and/or drug treatment remains unclear (Thompson et al. 2014). Therefore, the aim of the present study is to analyze the effect of 3 types of treatment – multicomponent exercise (E); oral hypoglycemic drug - metformin (M); combined therapy- exercise plus metformin (MEX) – on cardiovascular risk in older adults with type 2 diabetes (T2D), and with comorbidity in an early stage of the disease (HbA1c < 7.5 %).

Methods: This 2-year un-randomized longitudinal cohort study included 284 T2D older adults (> 60 years) that underwent one of 3 conditions: E (*n* = 59), trained three sessions per week; M (*n* = 30), used metformin 850 mg twice daily; MEX (*n* = 195), combined exercise plus metformin. Baseline and follow-up multifactorial cardiovascular risk assessment included anthropometric, hemodynamic components, lipid profile, glycaemia and cardiorespiratory fitness (CRF).

Results: After the 24-months of intervention, comparing E with M therapy, large effect sizes were observed in body mass (BM), waist circumference (WC), waist-to hip ratio (WHR), systolic (SBP), diastolic blood pressure (DBP) and cardiorespiratory fitness (CRF); body mass index (BMI) and glycaemia had moderate effet size.

Moreover, comparing MEX with M therapy, large effect sizes were found in BM, WC, WHR and CRF, and moderate effect sizes in BMI, SBP and DBP. E group decreased BM (3.6 %), WC (4.2%), BMI (2.7%), SBP (11.1%), DBP (11.3%), TG (21.2%), glycaemia (12.3%), and increased CRF (17.7%). M group increased WC (2.2%), WHR (3.1%), BMI (1.6%), and SBP (5.4%). MEX group reduced BM (1.1%), WC (2.4%), BMI (1.4%), and DBP (8.2%), while increased SBP (0.7%), glycaemia (6.7%), and CRF (18.0%).

Conclusions: Exercise training was the most effective therapy decreasing cardiovascular risk in early stage of T2D in older adults with multimorbidity, attenuating also some adverse effects of the M therapy.

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VITAMIN D STATUS MODULATES INNATE IMMUNE RESPONSES AND METABOLIC PROFILES FOLLOWING ACUTE PROLONGED CYCLING

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Keywords: neutrophil, elastase, inflammation, metabolomics

Introduction: The influence of vitamin D status on exercise-induced immunodepression remains unclear. The primary aim of our study was to investigate the effects of vitamin D status on innate immune responses to prolonged exercise. Secondly, we undertook a metabolomic profiling to suggest how the immune system may be modulated in relation to plasma 25(OH)D concentrations.

Methods: Twenty three healthy, recreationally active males (age 25 ± 7 years; body mass 76 ± 8 kg; height 179 ± 6 cm; maximal oxygen uptake [VO_2 max] 56 ± 9 $mL \cdot kg^{-1} \cdot min^{-1}$) completed 2.5 h of cycling at 15% Δ (~ 55-60% VO_2 max). Venous blood and unstimulated saliva samples were obtained before and after exercise. Based on available evidence, to date, on vitamin D status and innate immune responses (e.g. monocyte-derived cytokine production, plasma cathelicidin) in endurance athletes (He et al., 2013), participants were dichotimised using the following: plasma total 25(OH)D < 33 nmol/ L (low) or > 33 nmol/L (medium-high).

Results: Total lymphocyte count ($p = 0.013$) and neutrophil:lymphocyte ratio ($p = 0.033$), at rest, were lower in participants with low plasma 25(OH)D compared to those with greater plasma 25(OH)D, but the magnitude of exercise-induced changes in total and differential blood leukocytes, neutrophil-stimulated oxidative burst and salivary antimicrobial peptides were similar between groups ($p > 0.05$). Two-way mixed ANOVA revealed a significant main effect of group ($p = 0.010$) and a group ^{x} time interaction ($p = 0.003$) for bacterial-stimulated elastase release per neutrophil (neutrophil degranulation). Post hoc analysis of the low 25(OH)D group (pre-exercise: 100 ± 0 % pre-exercise, post-exercise: 83 ± 29; post-exercise: 58 ± 22) revealed a significant decrease from pre-exercise to 1 h post-exercise ($p = 0.007$), which at 1 h post-exercise was significantly lower compared with bacterial stimulated elastase concentration in those with higher plasma 25(OH)D (pre-exercise: 100 ± 0 % pre-exercise, post-exercise: 92 ± 20; 1 h post-exercise: 101 ± 31) ($p = 0.003$). Discriminant function analysis of plasma metabolomic profiles showed a clear separation of participants according to vitamin D status in post-exercise timepoints. Major sources of variation contributing to the effect of vitamin D status were markers

of inflammation (linoleic acid metabolites) and metabolites belonging to the functional class of the tricarboxylic acid cycle.

Conclusion: These findings provide evidence of the influence of vitamin D status on exercise-induced changes in parameters of innate immune defence, and markers of inflammation and metabolic stress.

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MODERATE ACTIVITY, NOT LIGHT OR VIGOROUS ACTIVITY, IS ASSOCIATED WITH A HIGHER PERCENT OF CIRCULATING CLASSICAL MONOCYTES POSITIVE FOR CX3CR1 AND CCR2

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The American College of Sports Medicine (ACSM) currently recommends adults perform at least 150 minutes per week of moderate physical activity. The PURPOSE of this preliminary analysis of an on-going study was to evaluate the relationship between the amount of moderate exercise and inflammatory receptors on monocytes. METHODS: To date, eight young adults (age mean±SE = 22.1±0.3 years) have completed all measurements. The subjects self-identified as being physically active (PA; n=4) or physically inactive (PI; n=4). PA subjects used planned physical activity to meet or exceed the ACSM recommendations, and PI subjects participated in no more than one day per week of regular physical activity. Subjects performed a two-stage estimated VO_2max test, wore an accelerometer (ActiGraph) for one week, and a post-absorptive resting blood sample was collected on the morning after the accelerometer data collection. Sodium heparinized whole blood

was used for lysed whole blood flow cytometery analysis, and serum was separated and stored at -80 degrees Celsius for later ELISA analysis of BDNF. Accelerometery data was analyzed with 1 second epochs and Freedson Adult VM3 (2011) cut points used to classify physical activity intensity. Pearson r values were calculated and included if $r>0.60$ and $p<0.05$. RESULTS: PA subjects a higher ($p=0.0345$) estimated VO_2max than PI subjects (PA 51.1±2.5 mL/kg/min; PI 34.8±3.4). There was no difference in average minutes per day of moderate activity between the two groups (PA 56.5±5.7 mins; PI 53.3±7.1) and all subjects exceed the ACSM recommendation of at least 150 minutes per week of moderate activity. Moderate activity was associated with BDNF ($r=-0.6841$ $p=0.0421$), percent of circulating classical monocytes positive for CX3CR1 ($r=0.7312$ $p=0.0393$), and percent of circulating classical monocytes positive for CCR2 ($r=0.8243$ $p=0.0118$). There were no associations between the variables of interest and light or vigorous activity. DISCUSSION: Despite the difference in reported days of planned physical activity, all PI and PA subjects exceeded the ACSM recommendation for moderate activity. However, PI subjects had higher estimated VO_2max, supporting their physically trained status. Moderate activity was positively associated with percent of circulating classical monocytes positive for CCR2, which may be related to the exercise-induced muscle damage signaling role of CCR2. Moderate activity was also associated with percent of circulating classical monocytes positive for CX3CR1, which may be related to exercise promoting a healthy immune system. CONCLUSSION: The preliminary results from this on-going study support an relationship between moderate activity and the immune system. The completed study will include monocyte function (LPS stims) and monocyte subset analyses to provide a more complete assessment of the relationship between physical activity and the immune system.

PERITONEAL MACROPHAGES AND ADIPOSE TISSUE MACROPHAGES POLARIZATION IN OBESE MICE: ROLE OF EXERCISE TRAINING AND PPAR-γ

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Keywords: Macrophages, exercise, inflammation, transcriptional factor.

Background: Moderate exercise training is increasingly consolidated as non-pharmacological therapy for the treatment and prevention of low-grade chronic inflammatory diseases. Macrophages are directly involved in the control of the inflammatory response and transcription factors such as peroxisome proliferator-activated receptor gamma (PPAR-γ) are able to regulate the immune-metabolic response targeting the increase of alternatively activated macrophages or M2, characterized by the secretion of anti- inflammatory cytokines. From the possibility of macrophage phenotype alteration due to the exercise, we intend to assess whether PPAR-γ deletion in myeloid cells can lead to impairment in the anti-inflammatory response of the exercise in a diet-induced state of low-grade inflammation. **Methods:** two animal strains were used: CreLox for PPAR-γ (KO) in myeloid cells and litter control animals (WT). Each genotype was divided into 3 subgroups 1) chow diet sedentary; 2) high fat diet sedentary (HF) 3) high fat diet and moderate intensity training (HFT). Were evaluated the metabolic profile of the animals, the inflammatory profile of peritoneal macrophages and subcutaneous adipose tissue through cytokine secretion/content (TNF-alpha, IL-6 and IL-10) and flow cytometry. The experimental protocol lasted 12 weeks (4w diet + 8w diet and training). **Results:** Peritoneal macrophages from KO mice seem to present a tendency to be proinflammatory as observed in increased TNF-α in non-stimulated and TNF-α and IL-6 in LPS-stimulated cells. The obesity induced by high fat diet did not alter inflammatory markers (figure 1) despite of increased IL-6 and IL-1β production in culture from WT group. Training by itself improved inflammatory parameters especially in WT animals also reducing TNF-α and IL-6 in LPS-stimulated cells from both genotypes. M1 markers were elevated in HFT animals (figure 1). On the other hand, adipose tissue-macrophages presented an anti-inflammatory profile at baseline conditions, increasing their cytokine content in HF WT animals and TNF-α, IL-1β and IL-10 in KO

mice. Exercise was able to reduce all proinflammatory cytokines in WT and only TNF-α and IL-1β in KO, otherwise, MCP-1 increased in trained KO mice as confirmed by M1 markers elevation. **Conclusion:** Adipose tissue-macrophages appear to be more susceptible to variations such as diet and/or exercise in the M1 or M2 polarization dynamics tham peritoneal macrophages, whereas PPAR-γ in these infiltrated macrophages seems essential for exercise-mediated anti-inflammatory effects.

NOVEL TIME-COURSE RELATED LINKAGES OF SKELETAL MUSCLE GENE NETWORKS WITH BLOOD INFLAMMATION AND MUSCLE DAMAGE MARKERS FOLLOWING ENDURANCE EXERCISE

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Key words: Muscle recovery, systemic inflammatory response, blood biomarker panels

Introduction: Network biology is an important new frontier in physiology that enables us, for example, to understand whether functional gene networks in tissues are related to clinically accessible blood markers (2). We previously analyzed the muscle and blood neutrophil transcriptomes in trained men at 3, 48 and 96 h after 2 h cycling and running (4,5). By applying weighted gene co-expression analysis (WGCNA) (3), an advanced network-driven method, to these data, we identified muscle gene networks that are co-expressed in neutrophils and correlated with inflammation markers (1). Expanding on these results, we specifically examined time-course related correlations of muscle gene networks with exercise-induced changes in blood

leukocyte counts, cytokines, high-sensitive C-reactive protein (hsCRP) and muscle damage markers.

Methods: WGCNA was performed to construct and analyze muscle gene co-expression networks based on data from pre- to 3 h, pre- to 48 h, and pre- to 96 h post-exercise. Relationships of the time-course related gene networks with blood variables were quantified by using the networks' eigengenes (3).

Results: The strongest correlations were identified between blood leukocyte counts, muscle damage markers, cytokine and hsCRP concentrations, and an acetylation- and mitochondria-related muscle gene network that was preserved from pre- to 3 h post-exercise. We also identified 5307 correlations ($P<0.05$) between blood variables and individual network genes including heat shock protein-encoding genes and nuclear factor interleukin 3 regulated. Furthermore, blood leukocyte counts, interleukin-6, hsCRP and plasma CK activity strongly correlated with a muscle network that was enriched with immune-related genes and preserved until 96 h post-exercise. 290 correlations ($P<0.05$) were identified between blood variables and individual genes of this latter network including the M1 macrophage 'marker gene' CD68, biglycan (BGN) and NCK-associated protein 1-like (NCKAP1L). BGN and NCKAP1L have specific roles in muscle-immune interactions and immune cell migration.

Discussion: The linkages of blood variables with muscle gene networks might reflect different phases of muscle recovery. These findings provide tentative evidence in support of the notion that a panel of predictive blood biomarkers may potentially help us to assess changes in the muscle, such as occurring during muscle recovery and remodeling following exercise. Such a biomarker panel may consist of more traditional physiological/biochemical/immunological variables combined with multi-gene biomarkers associated with a blood leukocyte/neutrophil gene network (1).

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A ROLE OF DAP12, AN ACTIVATING-TYPE IMMUNOREGULATORY MOLECULE IN SKELETAL MUSCLE REGENERATION.

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Key words: skeletal muscle, DAP12, M1/M2-type macrophage, ITAM.

Intruduction: Injured muscle regeneration and maintenance of skeletal muscle are integrated events by various related cells and humoral factors, but those regulatory mechanisms remain unclear. Recently, there are many reports on the involvement of immune cells in skeletal muscle regeneration, and it has been shown that not only the initiation of inflammation at the injured site but also direct involvement in the regeneration of injured muscle (Burzyn 2013). In this study, we focused on the activation signal adapter molecule DNAX activating protein of 12 kDa (DAP12), which was shown to be involved in cell differentiation and bone metabolism of myeloid cells (Koga 2004, Kaifu 2003). The purpose of this study was to examine whether DAP12 mediated signals in immune cells affect injured skeletal muscle repair and regeneration process.

Methods: Pharmacological muscle injuries using cardiotoxin were induced in the triceps surae muscle of C57BL/6 wild type and DAP12-deficient mice, and injured

muscle samples from the early to the recovery phase were sequentially collected. Thereafter, immunohistological analysis, flow cytometry analysis and qPCR gene expression analysis were performed.

Results: Retardation of muscle regeneration was observed in DAP12-deficient mice. In addition, F4/80+ cells localized in injured muscle were reduced in DAP12-deficient mice. Moreover, there was a change in the cell polarity of M1-/M2-type of F4/80+ cells in DAP12-deficient mice.

Conclusion: It was suggested that DAP12 mediated signals might be involved in the regulatory mechanism of skeletal muscle regeneration by controlling recruitment and differentiation of F4/80+ cells to injured muscles.

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INFLUENCE OF SPRINT INTERVAL EXERCISE AND CONTINUOUS AEROBIC EXERCISE ON CIRCULATING ANGIOGENIC LEUKOYCTES IN HEALTHY ADULTS

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Introduction: Although commonly understood as immune cells, certain T lymphocyte and monocyte subsets have angiogenic potential, contributing to blood vessel growth and repair.

Objective: To compare the effects of a single bout of continuous aerobic (CONEX) versus Sprint Interval Exercise (SIE) on circulating angiogenic leukocytes in healthy recreationally active adults.

Methods: Ten participants (aged 28.3±2.0 yr, weight 80±3.9 kg, BMI 25.4±0.95 kg/m^2) (mean±SEM) participated in the study. Participants completed, in a counterbalanced design, either 45 min of CONEX at 65-70% of maximum oxygen uptake or a SIE bout consisting of 6x20 sec cycle ergometer sprints. Blood was sampled pre-, post- (10 min), 2 h and 24 h post exercise for lysed whole blood flow cytometric analysis.

Results: Circa 45% of T lymphocytes and 25% of monocytes had an angiogenic phenotype, expressing the surface markers CD31 and Tie2 respectively. Circulating (cells/mL) CD3$^+$ T lymphocytes and CD3$^+$CD31$^+$ angiogenic T lymphocytes (T_{ANG}) were 63% and 50% higher respectively ($p<0.05$) post-exercise in SIE, but unchanged in CONEX. Values in SIE were back to pre-exercise at 2 h and 24 h. The increase in CD8$^+$ T_{ANG} was greater than CD4$^+$ T_{ANG} ($p<0.05$). The increase in CD3$^+$CD31$^-$ cells was greater ($p<0.05$) than the increase in CD3$^+$CD31$^+$ cells. Expression (mean fluorescence intensity) of the chemokine receptor CXCR4 on T_{ANG} was higher ($p<0.05$) at 24 h in CONEX but not SIE. There was a main effect of time on other markers. Compared to pre-exercise, circulating monocytes (CD14$^+$) were elevated ($p<0.05$) post- and 2 h post-exercise with Tie2 expression (MFI) on monocytes lower ($p<0.05$) at these timepoints. Endothelial progenitor cells were higher ($p<0.05$) post-exercise but at no other timepoint. Serum cortisol was lower ($p<0.05$) at 2 h and 24 h.

Conclusion: SIE is more effective than CONEX in increasing circulating T_{ANG} though CONEX may be more effective in increasing CXCR4 expression on T_{ANG}.

ELEVATED CORE TEMPERATURE: NOT ONLY USEFUL IN THE CONTEXT OF EXERCISE TO COMBAT CHRONIC LOW-GRADE INFLAMMATION?

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Keywords: passive heating; inflammatory response; heat shock protein 72; monocyte subsets; glucose control

Introduction: Regular exercise is suggested to be effective in reducing chronic low-grade inflammation, which in turn could enhance insulin sensitivity (1). Since the increase in body temperature during exercise is one of the proposed inducers of the beneficial acute inflammatory response, passive heating could be an alternative strategy to combat chronic low-grade inflammation in individuals without the physical capacity to engage in sufficient exercise (2). This study investigates both the acute inflammatory response to hot water immersion (HWI) as well as the chronic effects of a HWI intervention period. **Methods:** Nine sedentary, overweight (BMI: 31.0(4.3) kg/m^2), healthy males were immersed in water set at 39°C for 1 hour, whilst 1 hour of seated rest at ambient temperature was used as control condition. Blood was drawn from an antecubital vein pre, post and 2 hours post-session. A resting blood sample was taken 3 days after completion of a 2-week intervention period consisting of 10 HWI sessions (5 sessions of 45 min followed by 5 sessions of 60 min). Main outcome measures were monocyte intracellular heat shock protein 72 (iHsp72), the relative distribution of CD14++/CD16-, CD14++/CD16+ and CD14+/CD16++ monocyte subsets, plasma interleukin (IL)-6 concentration and fasting blood glucose concentration. **Results:** HWI increased rectal temperature from 37.0(0.7)°C to 38.8(0.4)°C. The concentration of IL-6 (p=0.048) and the percentage of CD14++/CD16+ (p=0.004) and CD14+/CD16++ (p=0.008) monocytes were significantly higher compared to control immediately post-HWI, whilst iHsp72 was not changed after HWI at any time point. Resting levels of IL-6 and iHsp72 were not changed following the intervention period. However, there was a trend for an increase in the percentage of CD14+/CD16++ monocytes (p=0.104) at rest and a

significant decrease in fasting glucose levels following the intervention (p=0.024). ***Conclusion:*** A single HWI session did induce an acute inflammatory response. This was, however, not accompanied by an acute elevation of monocyte iHsp72, possibly because the exposure to heat and the associated high rectal temperatures were not maintained for long enough. The 10 HWI sessions did not significantly alter the inflammatory markers at rest. Nevertheless, the lowering in fasting blood glucose concentration may indicate a positive change in glucose metabolism and/or insulin sensitivity, suggesting that HWI may induce some of the positive metabolic effects found after exercise training.

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BOVINE COLOSTRUM SUPPLEMENTATION ENHANCES SENSITIVITY OF THE IN VIVO IMMUNE RESPONSE TO A NOVEL ANTIGEN FOLLOWING PROLONGED EXERCISE

Authors

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Introduction: Prolonged exercise significantly reduces both the induction and elicitation of *in vivo* cell-mediated immune responses. The aim of the present study was to determine the effect of supplementation with bovine colostrum on *in vivo* immune induction using experimental contact hypersensitivity with the novel antigen DPCP.

Methods: In a double-blind design, 31 males were randomly assigned to either bovine colostrum (COL, 20 g/day, n = 15, age 23 ± 5 years, VO_2max: 57 ± 8 mL·kg^{-1}·min^{-1}) or placebo (PLA, n =16, age 25 ± 6 years, VO_2max 56 ± 5 mL·kg^{-1}·min^{-1}) for 58 days. Exactly 28 days into supplementation, participants took part in 2 h of running at 60% VO_2max. Within 20 min of exercise completion, all participants were sensitised to DPCP using a single patch applied to the mid-lower back for 48 h. Following the induction of immune-specific memory (sensitisation), participants reported to the laboratory 28 days later for a dose series of DPCP patches to be applied in a randomly allocated order to the volar aspect of their right upper arm for 6 h. Participants returned to the laboratory 24 h and 48 h following the application of patches for skin responses (oedema) to be measured at each DPCP patch site using modified skinfold callipers. Standardised diets (for the day pre-trial) and breakfasts (3.5 h pre-trial) were provided. Subjects were provided a 5 mL·kg^{-1} bolus of water 20 min before and immediately after exercise and 2 mL·kg^{-1} every 15 min during exercise.

Results: There was no difference in total oedema responses (sum of all skinfold sites) between COL (1.84 ±1.79 mm) and PLA (1.01 ± 0.92 mm, $p > 0.05$) at 24 h or 48 h (COL, 3.36 ±.3.32 mm; PLA, 2.83 ± 1.64 mm, $p > 0.05$). Analysis of the dose response curves allowed for the minimum dose (threshold) for a positive response in each group to be determined (i.e. sensitivity). Sensitivity at 24 h was 0.8 μg·cm^{-2} for PLA compared to 0.4 μg·cm^{-2} for COL, and at 48 h 0.7 μg·cm^{-2} for PLA compared to 0.4 μg·cm^{-2} for COL (i.e. greater sensitivity in COL). This was supported by greater oedema response ($p < 0.05$) to the lowest dose-response dose (which was 1.24

μg·cm^{-2}) in COL at 24 h and 48 h (0.22 ± 0.25 mm and 0.42 ± 0.50 mm, respectively) vs PLA (0.06 ± 0.11 mm and 0.16 ± 0.19 mm, respectively).

Conclusion: These findings suggest that COL enhances sensitivity of antigen-specific memory/cell-mediated immunity. Although there was no effect on the summed response, there were clear differences at the lowest dose and increased sensitivity in the COL group. Taken together this supports previous evidence from our laboratory where COL has been shown to act as a nutritional countermeasure to the decreased immunity (and increased susceptibility to illness) following prolonged exercise (e.g. Davison & Diment, 2010; Jones et al., 2014).

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EXERCISE AND SUPPLEMENTATION WITH TAURINE IN THE ELDERLY: EFFECTS ON IMMUNE AND BLOOD-BRAIN BARRIER INTEGRITY MARKERS

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Introduction: The blood-brain barrier (BBB) does not allow any bulk flow of substances between the blood and the brain, and acts as a ´´gate´´ that protects the neurons. Dysfunctions in this structure are directly associated with the appearance of neurodegenerative diseases, mainly in the elderly (Takeda, Sato and Morishita, 2014). The widening of inflammation and oxidative processes that occur with aging decrease the BBB integrity and contribute to increased degeneration (Elahy *et al.*,

2015). Both exercise and nutritional interventions have proven to be effective in promoting health benefits. However, their effects on the integrity of the BBB are still unknown. The objective of this work was to study the effect of exercise and supplementation with taurine on inflammatory cytokines and S100β and NSE levels. **Methods:** A total of 48 elderly women (age 83,58±6,9 years) participated in the study and were divided into four groups: combined exercise training (CET: n=13), taurine supplementation (TAU: n=12), exercise associated with taurine (CET+TAU: n=11) and control group (CG: n=12). CET was done 3 times per week, at 60-65% of MHR intensity. Taurine supplementation was given (1,5g/day) during 14 weeks. Interventions lasted 14 weeks and all subjects were evaluated before (T0) and after (T1) this period. The CG did not undergo exercise or supplementation programs. Plasma and serum concentrations of S100β, NSE, MPO, MMP-9, IL-10, IL1-ra, IL-1b, TNF-α and IL-17 were determined. RESULTS: Levels of IL-17 and S100β correlated in both moments ($p<0,01$). The CET group showed a subtle increase in IL-1ra and decrease in TNF-α and S100β levels (+33%, -15%, and -53%, respectively). The TAU group showed a decrease in IL-1b, MPO and MMP-9 levels ($p<0.05$), while no differences were observed for these variables in Ex+TAU between T0 and T1. S100β levels tended to increase only in the CG (+26%), and differences in this marker were observed between groups at T1 ($p<0,01$). **Conclusion:** Exercise alone promoted an anti-inflammatory effect. Nevertheless, decrease in MPO concentration was only observed in the groups supplemented with taurine. Combination of exercise and taurine did not promote significant added changes in inflammatory or oxidative stress markers when compared to the isolated interventions probably due to a compensation mechanism. However, exercise and taurine (alone or associated) promoted the maintenance of the S100β and NSE levels when compared to the CG, which suggests that, even in older ages, BBB structure may benefit from the exercise and taurine supplementation induced environment changes.

INFLUENCE OF VITAMIN D AND INFLAMMATION ON SLEEP DISORDERS IN SEDENTARY AND STREET RUNNERS

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Keywords: Apnea; runners; sedentary; inflammation

Introduction: Sleep is a functional state, reversible and cyclical.[1] Obstructive sleep apnea is a sleep disorder characterized by brief and recurring events of obstruction of the upper airway during sleep.[2] One of the most important actions of vitamin D is the control of the inflammatory response due to its potent immunomodulatory activity.[3] The aim of this study was to verify if serum levels vitamin D can influence sleep apnea syndrome in runners and sedentary. **Methods:** Fifty-three individuals living in the city of São Paulo were recruited, being twenty-seven runners and twenty-six sedentary. The study was approved by the ethics committee on human research of the Federal University of São Paulo under number 049494/2016. All participants responded Berlin Questionnaire, that assesses the risk of obstructive sleep apnea and it was attributed the number 1 to Berlin questionnaire result “without risk of apnea” and the number 2 to “with risk of apnea” to work with the statistical analysis. They also underwent peripheral blood analysis to measure vitamin D and high-sensitivity C-reactive protein (CRP_{HS}) **Results:** The analysis of Berlin questionnaire showed that 3.70% of the runners present a risk of apnea, while this percentage was 38.46% in the sedentary group (p=0.02). The comparison of vitamin D and CRP_{HS} levels between groups was analyzed and reveals that the concentration of vitamin D is higher in runners (27.22±5.9; 22.65±7.4; p=0.01) and the CRP_{HS} concentration is lower in the group of runners (0.14±0.1; 0.38±0.5; p=0.05). There was observed a negative correlation between the result of Berlin questionnaire and the Vitamin D levels (rho=-0.412, p<0.05). **Discussion:** Studies suggests that low vitamin D

predispose or aggravates obstructive sleep apnea, an inflammatory disorder.[4] However the prevalence of sleep apnea was significantly lower between runners, suggesting a positive effect of exercise in prevent this sleep disorder. The lowest values of CRP HS, can be assigned to the exercise itself and also to the low prevalence of sleep apnea between runners, taking into account that sleep apnea causes an inflammatory response. Otherwise, there is a correlation between higher levels of vitamin D and lower inflammatory response **Conclusion:** Our results suggests that inflammatory response, vitamin D levels and the quality of sleep are correlated. Otherwise the exercise seems to have a positive effect in reducing the risk of sleep apnea syndrome and to decrease the inflammatory response. Also exercise is associated with increased vitamin D levels, probably due to increased exposure to sunlight.

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RELATIONSHIPS BETWEEN CARDIORESPIRATORY FITNESS AND MARKERS OF SENESCENCE AND EXHAUSTION IN PERIPHERAL BLOOD CD8+ T-CELLS AND NK-CELLS

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Relationships between cardiorespiratory fitness and markers of senescence and

exhaustion in peripheral blood CD8+ T-cells and NK-cells in the context of latent cytomegalovirus infection: preliminary findings from the Texas City Stress and Health Study

Lifelong infection with the beta-herpesvirus, cytomegalovirus (CMV), may contribute to immune cell exhaustion and the premature acquisition of a senescent phenotype. Regular exercise is considered a viable behavioral intervention to improve latent viral control and prevent the early onset of immunosenescence. We examined relationships between cardiorespiratory fitness (VO_{2max}) and markers of exhaustion (PD-1) and senescence ($p16_{INK4a}$) in peripheral blood T-cells and NK-cells obtained from 317 respondents of the Texas City Stress and Health Study; a large (n = 1,455, 58.4 percent female; age 25-91 years) tri-ethnic community located on the southwest shoreline of Galveston Bay, Texas. VO_{2max} was estimated using non-exercise equations that incorporate physical activity rating, body-mass index, age and sex. PD-1 and $P16_{INK4a}$ were measured in cryopreserved CD8+ T-cells and NK-cells by 8-color flow cytometry as part of an ongoing comprehensive immunophenotyping panel. CMV serostatus and optical density (surrogate measure of viral load) was determined by ELISA. The expression of $p16_{INK4a}$ in both CD8+ T-cells and NK-cells was inversely associated with VO_{2max}. Moreover, Those with higher VO_{2max} had a lower expression of PD-1 on CD8+ T-cells but not NK-cells. These findings were independent of both CMV serostatus and CMV viral load. However, CMV viral load was positively associated with PD-1 expression on both CD8+ T-cells and NK-cells, and also with $p16_{INK4a}$ in CD8+ T-cells. The relationships between CMV viral load and PD-1 expression was strongest in those aged 45-64 years, whereas the relationship with $p16_{INK4a}$ was strongest in those older than 65 years. In conclusion, these preliminary findings have revealed associations between VO_{2max} and the composition of exhausted and senescent CD8+ T-cells and NK-cells, thus advocating exercise as a viable behavioral intervention to offset age-related declines in immune function. Further analysis of this data set will provide important information on the possible protective effects of cardiorespiratory fitness on the premature acquisition of a senescent phenotype in the context of latent herpesvirus infections, low-grade inflammation and a host of psychosocial factors.

CHRONIC RESPONSES OF INFLAMMATION AND MACROPHAGE FUNCTION TO EXERCISE TRAINING IN VARIOUS TISSUES OF SENESCENCE MICE

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Keywords: Age-related chronic inflammation, macrophage, resistance training

Introduction: Aging induces chronic inflammation in whole-body and this chronic inflammation is associated with immune dysfunction. Moreover, the local inflammation is induced by macrophage infiltration and polarization and leads to several diseases, such as alzheimer's disease, cardio vascular diseases and metabolic disorders (Freund A, et al., 2011). Regular aerobic exercise reduces circulating levels of inflammatory markers, such as IL-6 and TNF-α, in animal and human (Liao P H et al., 2015). However, the effect of different exercise manner on chronic inflammation in various tissues with agingremains unclear. The aim of this study was to investigate the effects of resistance and aerobic training on chronic inflammatory responses and macrophage infiltration and polarization in various tissues of senescence mice. **Methods:** Male 38-week-old senescence accelerated prone mouse 1 (SAMP1) mice, as a mouse model of accelerated senescence, were randomly divided into three groups: sedentary-control (Aged-con), aerobic training (Aged-AE), and resistance training (Aged-RT). After 12-week interventions, mRNA expression of inflammatory cytokines (TNF-□ and IL-6) and macrophage markers (F4/80, CD11c and CD163) in various tissues were assessed by real-time RT-PCR with Taqman probe. Additionally, male 25-week-old SAMP1 mice were used as sedentary-control (Young-Con). **Results:** in Aged-Con group, mRNA expression of TNF-□ in brain, adipose tissue, blood vessel, heart, liver and small

intestine significantly increased as compared with Young-Con group. However, these mRNA expressions in Aged-AE and Aged-RT groups wereattenuated and these expression levels were not differed with Young-Con group. Additionally, no significant difference of IL-6 mRNA in each organ among four groups was observed. Thus, aging-induced chronic inflammation in various tissues may be attenuated by aerobic and resistance training In the chronic inflamed tissues of Aged-Con group, F4/80 mRNA expression was significantly or slightly higher than that of Young-Con group, but did not change in the brain. In contrast, F4/80 mRNA expression in these tissues of Aged-RT and Aged-AE group significantly reduced as compared with Aged-Con group. Furthermore, aging-induced increased in ratio of CD11c / CD163 mRNA expression was attenuated by resistance and aerobic exercise training. **Conclusion:** These results indicate that resistance and aerobic training might prevent the chronic inflammation in various tissues with advancing age, and this phenomenon might be related to the change in the macrophage infiltration and polarization.

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EXERCISE, THE MICROBIOTA AND IMMUNE REGULATION

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Introduction Exercise and the microbiota exert strong influence on the immune system. Evidence from animal models suggests that exercise may alter the composition of the microbiota, suggesting a further mechanism to explain the beneficial effects of physical activity [1]. We examined differences in faecal microbial composition and whole blood immune cell profiles between healthy adults, well trained recreational athletes and a cohort of elite athletes selected for the Rio 2016 Olympics. **Methods** A cross-sectional study compared gut microbiota and peripheral blood immune cell profiles in 12 healthy adults (age 42 ± 11 yrs; body mass index (BMI) 22 ± 1.2 kg/m^2; mean ± SD), 12 well-trained recreational athletes (age 27 ± 6.3; BMI 22 ± 2.0 kg/m^2) and 12 elite athletes selected for the Rio 2016 Olympic Games (age 24 ± 3.62, BMI 23 ± 1.5 kg/m^2). Peripheral blood innate and adaptive immune cell abundance was determined by the nCounter® PanCancer Immune Profiling panel (NanoString Technologies, WA, USA). Microbiome composition was assessed using 16s rRNA gene sequencing. **Results** Preliminary analysis indicates a significantly greater diversity of microbes in elite and recreational athletes compared to healthy individuals. Elite athletes displayed a considerably smaller variation in total microbial diversity compared to both recreational athletes and healthy individuals. Elite athletes had significantly lower abundance of CD8$^+$, exhausted T-cells, NK cells (dim) and Th-1 cells. Both recreational and elite athletes had a significantly lower abundance of macrophages than healthy individuals. Recreational athletes had a significantly higher abundance of regulatory T cells,

dendritic cells and Th-2 cells than elite athletes and healthy individuals. **Discussion** Differences in immune and microbial composition between the groups was evident, with elite athletes characterised by a Th-1 profile and recreaational athletes by a Th-2 profile. Further analysis on the relationship between microbial operational taxonomic units and immune cell subsets may provide further information in humans for an exercise – diet interaction in relation to gut bacteria.

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ANALYSIS OF MODERATE AEROBIC EXERCISE ON THE GUT MICROBIOTA FROM MICE INDUCED TO OBESITY WITH HIGH FAT DIET.

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Obesity is a multifactor disease associated with a high rate of mortality and morbidity worldwide. The gut microbiota is shown to be a key factor in the pathogenesis of obesity influencing the host metabolism. Diet and exercise were shown to modulate the gut microbiota (Bermon et al., 2015, Petriz et al., 2014, Kang et al., 2014), however, this relation is still poorly understood. The present study was conducted to better understand the effect of aerobic exercise on the gut microbiota in animal model submitted to an obesity-inducing diet. Forty isogenic male C57Bl/6J mice were divided into two groups; low-fat diet (10%-LF, n=20) and high-fat diet (60%-HFD, n=20). After 16 weeks, all animals were submitted to four weeks of acclimatization and exercise adaptation to the treadmill apparatus. Furthermore, mice were divided into four groups; low-fat training (LFE n=10), low-fat control (LFC, n=10), high-fat training (HFE, n=10) and, high-fat control (HFC, n=10). All animals were submitted to a maximal velocity incremental test (Vmax) for assessing the training intensity, set as 50% of Vmax, during 30 $min.d^{-1}$, 5 days/week, for 8 weeks. For transcriptomic analysis, fecal content was collected prior to pre-dietary control, prior to the training program and after 8 weeks of training. Next Generation Sequencing Illumina MiSeq System of the 16S RNAr was used to analyze the effect of high-fat diet and training on the gut microbiota. The HF diet group presented a significant weight gain compared to the LF group, (~8,71g, $P<0.0001$). Training resulted in weight loss of the HFT group (39,1g, $P<0.05$), compared to the HFC group (44,3g, $P<0.05$). Moreover, Vmax in LFT group was improved after 4 weeks of training (26.1 $m.min^{-1}$, $P<0.05$), also reaching a longer distance (375.4m, $P<0.01$) compared to the LFC group (240m, $P<0.0001$). All DNA samples were successfully amplified. NGS is still in analysis, however, physiologic data indicated that the proposed exercise program didn´t lead to improvement in aerobic capacity in the HFE group. Despite the weight reduction due to training, the continuous HF diet may have negatively influenced animal's performance.

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ABSTRACT POSTERS

13th Symposium of the International Society of Exercise and Immunology

1 - MODIFICATIONS IN HAEMATOLOGICAL INDICES OF UNIVERSITY ATHLETES FOLLOWING SOCCER COMPETITION

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Modifications in haematological indices have shown to be influenced through involvement in soccer competitions. These modifications have not been established among Ghanaians youth who engage in soccer competitions. This study therefore documents the modifications in haematological indices through participation in football competition of university athletes in Ghana.

Haematological indices of fasting plasma glucose (FBS), haemoglobin (HBG), Red blood cell (RBC), haematocrit (HCT), mean cell volume (MCV), mean cell haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), white blood cells (WBC), neutrophils (NEUT), lymphocytes (LYM), absolute content of leucocyte (MXD♯), erythrocyte (ERT) and platelets (PLT) of ten university soccer players (mean age = 22.90 ± 1.79years) were examined before and after two weeks of intense national university soccer competition.

Results show significant decrease in RBC (13.26%, p =.003), HCT (7.69%, p =.019), MXD♯ (60.71%, p=.009) and ERT (46.15 %, p = .005). Significant increases were however observed in MCV (5.50%, p = .000), MCH (11.59%, p= .001), MCHC (5.95%, p = .032) and WBC (35.97 %, p= .000).

It was concluded that, university soccer players could only perform optimally during competition with appropriate dietary interventions to prevent iron deficiency, vitamin depletion, hypochlorhydria, and protein malnutrition and complications like long-standing respiratory distress.

2 - EFFECT OF DIFFERENT LOADS OF TREADMILL EXERCISE ON TH1/TH2 BALANCE OF ISOLATED SPLENOCYTES IN RAT

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Keywords: Moderate exercise, splenocyte, Overtraining, Immune system, Th1/Th2 balance, Rat

It has been shown that the imbalanced immune system with poor Th1 and overactive Th2 responses can result in a wide variety of chronic illness and cancer (1). In this study the effect of moderate and overtraining exercise on Th1/Th2 balance was evaluated in rat isolated splenocytes. Male Wistar rats were randomly divided into sedentary control (C), moderately trained (MT), (V=20 m/min, 30 min/day for 6 days a week, 8 weeks), overtraining (OT) (V=25 m/min, 60min/day for 6 days a week, 11 weeks) and recovered overtraining (OR) (OT plus 2 weeks recovery) groups, (n=6 for each group). At the end of study, cell viability, proliferation, interleukin 4 (IL-4) and interferon-γ (IFN-γ) secretion in non-stimulated, phytohemagglutinin (PHA) and concavaline A (Con A)-stimulated splenocytes were evaluated. Cell viability of stimulated and non-stimulated splenocytes increased in MT and OR groups compared to control group ($p<0.01$-$p<0.001$). Only cell proliferation of stimulated and non-stimulated splenocytes from OR group was higher than other groups ($p<0.01$-$p<0.001$). There were not significant differences in IL-4 concentrations between non-stimulated splenocytes isolated from different groups. IL-4 concentrations of PHA-

stimulated cells from MT and OT groups, as well as, IL-4 concentrations of Con A-stimulated cells from OR and OT groups were higher than the control group ($p<0.05$-$p<0.001$). There were not significant differences in non-stimulated and stimulated cell IFN- γ concentration between groups. In non-stimulated cells, IFN- γ / IL-4 ratio of OR group was higher than MT and OT groups ($p<0.05$-$p<0.01$). In PHA and Con A-stimulated cells, IFN- γ / IL-4 ratio was lower in exercise groups than control ($p<0.05$-$p<0.001$). Although we previously showed that moderate exercise increase Th1 cytokines in serum (2), but in splenocytes Th2 or Th1 response may increase depending the type of mitogen stimulation. Two weeks recovery restored Th1/Th2 balance, only in non-stimulated splenocytes of overtrained animals.

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3 - THE EFFECT OF PROLONGED REPEATED MODERATE INTENSITY EXERCISE ON CYTOKINE CONCENTRATIONS IN ADULTS

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Keywords: Myokines, IL-6, TNF-alpha,

ABSTRACT

Purpose: Previous studies showed that cytokine concentrations are affected by the intensity and duration of one bout of exercise (1, 2). The cytokine responses after

consecutive days of exercise have not been studied before, nor whether the responses differ between men and women. Therefore, the aim of this study was to asses cytokine responses after repeated bouts of exercise and compare those responses between men and women. **Methods:** 50 male (58.9 ± 9.9 years old) and 50 female (50.9 ± 11.2 years old) individuals were measured during four consecutive days of walking exercise. Participants walked 30, 40 or 50km, at a self-selected pace. Blood samples were collected one or two days prior to the start of the exercise (baseline) and at every walking day post-exercise. Blood samples were analysed for IL-6, IL-8, IL-10, IL-1beta and TNF-alpha concentrations. **Results:** All cytokine concentrations increased from baseline to post-exercise at day 1 ($p < 0.001$). These concentrations significantly decreased from day 1 to day 2 ($p < 0.001$), except for IL-1beta. IL-10 was higher in men than in women after the 1st day of exercise, IL-6 was higher in men after the 2nd day, and IL-1beta and TNF-alpha were higher in men during all days. **Conclusion:** The exercise-induced change in cytokines after day 1, attenuated on subsequent days. Men and women showed different baseline levels and similar exercise responses. These results suggest that muscles adapt rapidly to this type of exercise.

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Authorships

The study was designed by R. Terink, C.W.G. Bongers, M.T. Hopman, and M.R. Mensink; data were collected and analyzed by R. Terink and C.W.G. Bongers; data interpretation and manuscript preparation were undertaken by R. Terink, C.W.G. Bongers, M.T. Hopman, R.F. Witkamp, M.R. Mensink, and J.M.T. Klein Gunnewiek. All authors approved the final version of the paper.

Declaration

We declare that the results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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4 - COMPARABLE NEUTROPHIL RESPONSES FOR ARM AND INTENSITY-MATCHED LEG EXERCISE

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Keywords: upper body exercise, neutrophilia, CXCR2, IL-8, neutrophil degranulation

Introduction: Arm exercise is performed at lower absolute intensities than lower body exercise. This may impact on intensity dependent neutrophil responses and it is unknown whether individuals restricted to arm exercise experience the same neutrophil response as found for lower body exercise. Therefore, the aim of this study was to determine the importance of exercise modality and relative exercise intensity on the neutrophil response. **Methods:** Twelve moderately trained males performed three 45-min constant load exercise trials following determination of peak oxygen uptake for arm exercise ($\dot{V}O_{2peak\ arms}$) and cycling ($\dot{V}O_{2peak\ legs}$): (1) arm cranking exercise at 60%$\dot{V}O_{2peak\ arms}$; (2) moderate cycling at 60%$\dot{V}O_{2peak\ legs}$; and (3) easy cycling at 60%$\dot{V}O_{2peak\ arms}$. Blood samples were taken before exercise and in the 4 h recovery period. **Results:** Neutrophil numbers in the circulation increased for all exercise trials, but were significantly lower for easy cycling when compared with arm exercise (P=0.009), mirroring the blunted increase in heart rate and adrenaline during easy cycling. For all trials, exercising heart rate explained some of the variation of the neutrophil number 2h post exercise (R=0.51-0.69), adrenaline explaining less of this variation (R=0.21-0.34). Stimulated neutrophil elastase release was reduced in the recovery period for all trials (P<0.02), with no difference between trials (P=0.53). The number of neutrophils expressing CXCR2 decreased in the

recovery from exercise in all trials (P<0.05). **Conclusion:** Arm and leg exercise elicits the same neutrophil response when performed at the same relative intensity, implying that populations restricted to arm exercise might achieve a similar exercise induced neutrophil response as those performing lower body exercise. A likely explanation for this is the higher sympathetic activation and cardiac output for arm and relative intensity matched leg exercise when compared with easy cycling, which is partly reflected in heart rate. This study further shows that the downregulation of CXCR2 may be implicated in exercise-induced neutrophilia.

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5 - EFFECTS OF CAFFEINE SUPPLEMENTATION ON CYTOKINE RESPONSE TO A TREADMILL EXERCISE TEST

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Caffeine is commonly used by endurance athletes to improve performance (Graham 2001). In addition to the ergogenic effects, it has been suggested that caffeine could influence the cytokine response to exercise (Tauler et al. 2013). The aim of this study was to determine the effects of caffeine supplementation on plasma levels of cytokines, mainly IL-10 and IL-6, in response to exercise.

In a randomized, double-blinded study design, thirteen healthy well-trained recreational male athletes performed, on two different occasions, a treadmill exercise test (60 minutes at 70% of maximal oxygen uptake) 60 minutes after ingesting 6 mg/kg body mass of caffeine or placebo. Blood samples were taken before exercise, immediately after finishing the exercise and two hours after finishing the exercise. Plasma concentrations of IL-10, IL-6, IL-1beta, IL-1ra, IL-4, IL-8, IL-12 and IFN-gamma were determined using commercially available ELISA kits. Plasma cortisol and cAMP levels were determined as well.

Exercise test induced significant increases in IL-10, IL-6, IL-1beta, IL-4, IL-8, IL-12 and IFN-gamma plasma levels. Caffeine supplementation influenced only IL-6 and IL-10 levels, with higher concentrations in response to exercise. Furthermore, after recovery, IL-10 levels in control participants returned to basal levels, but remained high in supplemented participants. Caffeine supplementation induced higher cortisol levels after exercise but did not influence plasma cAMP levels.

Changes observed in IL-6 and IL-10 in response to exercise and caffeine supplementation are in agreement with previous results obtained during a simulated 15-km run competition (Tauler et al. 2013). These results indicate a significant influence of caffeine supplementation on the response of two important cytokines such as IL-6, which has been proposed as the key factor in the response to exercise (Pedersen et al. 2004), and IL-10, one of the main anti-inflammatory cytokines, to exercise. However, and in spite of a possible contribution of cortisol, mechanisms involved remain to be elucidated.

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7 - RELATIONSHIP BETWEEN THE STABILITY AND EMOTIONAL STABILITY OF SPORTS PERFORMANCE AND CHANGES IN GUT MICROBIOTA WITH MENTAL AND PHYSICAL STRESS

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Aim: In this study, we investigated in university male long-distance runners whether the classification of gut microbiota changed according to an athlete's subjective condition. In addition, we used the Big-Five Factor Markers of personality traits to investigate whether changes in the intestinal microbial flora were related to emotional stability, with the aim of obtaining basic material useful for the field.

Method: Forty-one male long distance athletes (mean age, height, weight and 5000m performance; 19.9 ± 3.0 year, 171.6 ± 5.0 cm, 58.1 ± 2.6 kg and 15'31 ± 31") participated in this study. The athletes were asked to take two stool samples for gut microflora analysis, one while in a "normal" condition (decided subjectively) and one when in a "worse" condition, excluding physical conditions such as when clearly affected by a common cold. Gut microbiota were classified by terminal restriction fragment length polymorphism analysis. The performance stability of each athlete

was evaluated from changes in his competition performance and usual training record, assessed by the athlete's coach using a ten-point subjective evaluation. We examined the relationship between emotional stability and performance stability using the Big-Five Factor Markers inventory.

Results: There was a significant correlation between emotional stability and performance stability ($r=0.621$, $p<0.05$, $n=41$). Based on this result, the athletes were divided into high emotional stability and low emotional stability groups, and the amount of change in the gut microbiota classification between the "normal" condition and "worse" condition stool samples were examined. **Conclusions:** There was no significant difference between the two groups in the amount of change in the intestinal microbial community. However, the data suggested that the gut microbiota differs greatly between individuals. Further investigation of the relationship between detailed changes in gut microbiota and individuals' mental and physical condition is warranted.

8 - CAN INTERVALS ENHANCE THE INFLAMMATORY RESPONSE AND ENJOYMENT IN UPPER-BODY EXERCISE?

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Keywords: affect; upper-body exercise; high-intensity interval training; chronic low-grade inflammation; Interleukin-6

Introduction: Compared to lower-body exercise, the acute inflammatory response to upper-body exercise might be attenuated as a result of the smaller muscle mass involved (1). Since populations for which upper-body exercise is most suitable (e.g. wheelchair users) are generally also at an increased risk for the development of a chronic low-grade inflammatory state, it is of interest to explore forms of upper-body exercise that could potentiate the acute inflammatory response. Since exercise has to be performed on a regular basis to experience its benefits and adherence rates

might be affected by the perceptual responses to exercise (2), this study investigates both the inflammatory as well as the perceptual responses to 3 different forms of upper-body exercise, with a particular focus on high-intensity interval training (HIIT) as an alternative exercise mode. **Methods:** Twelve recreationally active, able-bodied males performed 3 work-matched arm-crank trials in a randomised order: 30 min moderate-intensity continuous (CON), 30 min moderate-intensity with changes in cadence (CAD) and 20 min HIIT. Blood samples were taken pre, post and 2 h post-exercise to determine the plasma concentrations of interleukin (IL) -6 and IL-1ra. Perceptual responses pre, during and after exercise were assessed using the Feeling Scale, Felt Arousal Scale, Ratings of Perceived Exertion (RPE) and the Physical Activity Enjoyment Scale (PACES). **Results:** All trials were evenly effective in inducing an acute inflammatory response, indicated by increases in IL-6 after exercise (p<0.001) and in IL-1ra at 2 h post-exercise (p=0.003), without differences between the trials (p>0.29). More negative affect and higher RPE were reported *during* HIIT compared to CON and CAD, whereas PACES scores as reported *after* exercise were higher for HIIT and CAD compared to CON (p=0.005). **Conclusion:** When matched for external work, there was no difference in the inflammatory response to HIIT compared to moderate-intensity upper-body exercise. Although HIIT was (perceived as) more strenuous and affective responses were more negative *during* this trial, the higher ratings of enjoyment for both HIIT and CAD reported *after* exercise suggest that the inclusion of variation might enhance enjoyment in upper-body exercise. As the fashion in which upper-body exercise is performed does not seem to influence the inflammatory response, it might be advised to prescribe varied exercise to enhance its enjoyment.

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9 - POTENTIAL OF TEAR FLUID ANTIMICROBIAL PROTEINS TO EVALUATE RISK OF UPPER RESPIRATORY ILLNESS

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Keywords: Tear biomarkers, Infection, Immune, Non-invasive, Monitoring

Transmission of upper respiratory tract infections (URTI) has been demonstrated at the ocular surface (Bischoff et al., 2011). Thus, the immunological profile of the tear fluid likely plays an important role in host defence against URTI, and moreover provides a non-invasive medium for assessment of immune status. We recently demonstrated that tear secretory IgA (SIgA) has potential as a biomarker of URTI risk (Hanstock et al., 2016). It is likely that several other antimicrobial proteins abundant in tears such as lactoferrin (Lf) and lysozyme (Lys) contribute to host defence at the ocular surface (McDermott, 2013).

Purpose: To explore the potential of tear Lf and Lys to evaluate risk of subsequent URTI independently and in combination with tear SIgA data from the same subjects presented in Hanstock et al., (2016).

Methods: Forty healthy, physically active subjects were recruited during the common-cold season. Subjects reported upper respiratory symptoms (URS) daily and provided weekly tear samples for 4 weeks. If URS were reported for ≥ 48h, subjects provided a nasopharyngeal swab for identification of common-cold pathogens using RT-PCR and a tear sample. Following an episode of URS, subjects reported daily URS until they had been symptom-free for 4 weeks at which time a 'Recovery' tear sample was collected. Tear Lf and Lys concentration was determined using ELISA.

Results: Eleven subjects reported episodes of URS; nine of whom returned positive virology tests for human rhinovirus (URTI). Twenty-two subjects remained symptom-free during the monitoring period (Healthy) and seven were excluded due to non-compliance. Tear Lys concentration (Lys-C) and secretion rate (Lys-SR) were lower in URTI vs. Healthy ($p<0.01$ and $p<0.05$) but there was no difference in Lf-C and Lf-

SR. The potential of Lf and Lys to assess URS risk was determined by comparing Lf and Lys the week before URS with Recovery samples. Tear Lf-C, Lf-SR and Lys-C were not altered before URS, whereas Lys-SR tended to be reduced in the week before URS ($p<0.1$). A binary logistic regression incorporating tear flow rate, Lys-C, Lf-C and SIgA-C as predictors was able to correctly identify subjects at risk of URS in the next week with 70% accuracy (95% CI: 54 – 85%) but only 27% sensitivity.

Conclusion: Although tear Lys was decreased during URTI, the new model including tear Lys and Lf was not able to improve upon the utility of tear SIgA alone to assess URS risk in this small cohort. Larger datasets will be required to evaluate and optimise model performance for models based on tear SIgA, possibly in combination with other biomarkers, to predict URTI.

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10 - THE EFFECT OF PROFESSIONAL SPORT TRAINING ON CIRCULATING MARKERS OF ASEPTIC VASCULAR INFLAMMATION

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Keywords: nitric oxide, nitrotyrosine, inflammation, lipid profile, wrestlers

Introduction. Vascular inflammation is an early marker of endothelial dysfunction prior to the development of structural changes and clinical symptoms, contributes to

the progression of atherosclerosis, and increases the risk of coronary events. Studies over the past year have demonstrated the significance of inflammation in endothelial apoptosis which can be caused by high level of various pro-apoptotic factors such as tumour necrosis factor (TNFα), nitric oxide (NO) and 3-nitrotyrosine (3-Nitro), free and oxidised low-density lipoproteins (oxLDL) generated during long-term intense exercise. Endothelial dysfunction resulting from elevated inflammatory and pro-apoptotic mediators has been implicated in cardiovascular diseases (CVD) [Föstermann 2010, Gardner et al. 2014, Hirata et al. 2010]. We examined the effects of sport training on pro-apoptotic factors and their interaction with vascular inflammation.

Materials and Methods. Blood samples were collected from elite Greco-Roman wrestlers (*n*=16) during preparatory period for the new season (pre-season, January) as well as from non-athletes(*n*=12).

Results. NO concentration did not differ between groups while TNFα, 3-Nitro, oxLDL and hsCRP were significantly higher in wrestlers compared to non-athletes. Wrestlers showed the high levels of TNFα, 3-Nitro, hsCRP, total cholesterol (TC), LDL lipoproteins and atherogenic coefficient (AC). 3-Nitro concentration correlated with hsCRP (r=0.609, $p<0.001$), LDL (r=0.381, $P<0.05$) and AC (r=0.408, $p<0.001$).

Conclusion. The findings suggest that sport training may be associated with higher levels of pro-apoptotic mediators are related to other conventional CVD risk factors.

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11 - DOWNHILL EXERCISE INDUCES INCREASE OF INFLAMMATORY CYTOKINES IN TRICEPS BRAQUII OF MICE WITH OPPOSITE RESPONSE BETWEEN IL-4 AND IL-13 AT 72 HOURS AFTE

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Background: In large models of skeletal muscles damage, the participation of inflammatory cytokines are clearly temporal and divided in two distinct processes: the injury and regenerative stages. In the injury stage, the secretion of pro-inflammatory cytokines is mandatory and its are one of responsible for amplification of lesion process with concomitant action on proliferative response of fibrogenic and myogenic cells. In later stages, the regenerative process is characterized by the switch of inflammatory profile of muscle damage, upregulating the secretion of antiinflammatory cytokines, which are able to support the myogenesis. However, exercise-induced lesions are smaller when compared with other injuries models, and besides to stabilize the inflammatory response, this kind of inflammation also leads to an important muscles adaptations. **Objective** : Based on this, the aim of this study was identify when different classes of citokynes are release after exercise-induced muscle damage (EIMD). **Methods:** Thirty-six C57BL/6 mice were exposed to an experimental protocol of downhill exercise (18 bouts, speed 16 mts/min, during 5 min at -16º of inclination, each bout was followed by 2 min of interval passive rest) and then, mice were euthanized 0, 24, 48 and 72 hours after the exercise. Control group was not carry out the exercise and was euthanized in the same time with the experimental group. The triceps braquii (TB) muscle were dissect, submitted to protein extraction, followed by cytokines analyses. The muscular Interleukin-1 beta (IL-1β), IL-6, tumoral necrosis factor-alpha (TNF-α), monocyte chemoatractive protein-1 (MCP-1), interferon gamma-1(IFN-$_{\gamma}$), IL-4 and IL-13 were determined by multiplex assay. RESULTS: Downhill exercise was responsible to increase the pro-inflammatory cytokines secretion 3 days after EIMD compared with control group (P≤0,05), to decrease the IL-4 (P≤0, 05, compared to 0 hours group) and increase

the IL-13 (P≤0, 05, compare to control); an antiinflammatory TH-2 cytokine type. **Conclusion**: the changes of inflammatory profile after EIMD are not clear to observed. It might happen because the muscle structural modification in exercise-induced damage is not large, which facilitates the elevation of growth and antiinflamatory molecules, even in an environment predominantly composite by pro-inflammatory cytokines. Futhermore, this increase of IL-13, three days after exercise may represent an important antiinflammatory turning point in TB muscle of mice after dowhill exercise protocol.

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12 - EFFECTS OF CAFFEINE SUPPLEMENTATION ON LPS-INDUCED EX VIVO CYTOKINE PRODUCTION FOLLOWING EXERCISE

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Keywords: exercise; caffeine; LPS; cytokines

The capacity of leukocytes to produce cytokines upon adequate challenge is highly likely to reflect the capacity of an individual to defend itself against intruding microorganisms (Abbasi *et al.*, 2013). Because immune cells are one of the targets of caffeine (Horrigan, Kelly and Connor, 2006), the aim of this study was to determine

the effects of caffeine supplementation and exercise on the capacity of whole blood cultures to produce cytokines in response to endotoxin (LPS).

In a randomized, double-blinded study design, thirteen healthy well-trained recreational male athletes performed, on two different occasions, a treadmill exercise test (60 minutes at 70% of maximal oxygen uptake) 60 minutes after ingesting 6 mg/kg body mass of caffeine or placebo. EDTA blood samples were taken before exercise, immediately after finishing the exercise and, also, two hours after finishing the exercise test. Whole blood was incubated with or without LPS for 24 h, and cytokine concentrations (IL-10, IL-6, IL-8, IL-1ra and TNF-alfa) were determined in the culture supernatants using commercially available ELISA kits. Monocyte numbers were used to normalize cytokine production (difference between cytokine concentration in stimulated and unstimulated cultures) in a per cell basis (Abbasi *et al.*, 2013).

Exercise influenced cytokine culture concentrations, with non-significant increases in IL-10, IL-6 and IL-8 after exercise. However, when the normalized to monocyte number values were considered, no effect of exercise was observed. IL-1ra culture concentration increased after exercise, with higher values after recovery. However, IL-1ra production increased significantly only after recovery. Nor TNF-alfa concentration neither its production was affected by exercise. No significant effects of caffeine supplementation were observed throughout the study.

In conclusion, exercise test performed induced a modest influence on endotoxin induced cytokine production in whole blood cultures, with slight increases after exercise. Supplementation with 6 mg/kg body mass of caffeine did not influence the stimulated production of cytokines considered.

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13 - CHANGES IN INFLAMMATORY MOLECULES FOLLOWING MODERATE INTENSITY CONTINUOUS AND HIGH INTENSITY INTERMITTENT ACUTE EXERCISES IN YOUNG HEALTHY MEN

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Keywords: Cytokines, Exercise, Intensity

Introduction and objective: Currently, many studies has been showed a possible role of physical exercise in the modulation of inflammatory response[1,2]. However, there is very few dataevaluating different intensity iso-work protocols in regard to the effects on inflammatory molecules.Therefore, in this study we evaluated urinary and plasma levels of cytokines following high and moderate intensity protocols of physical exercise. **Subjects and methods:** Thirteen young healthy physically active men attended to four supervised training sessions. Two evaluation sessions were performed to measure body composition, physical activity, aerobic and anaerobic capacities before High Intensity Interval Exercise (HIIE) and Moderated Intensity Continuous Exercise (MICE) iso-work exercise sessions on a cycle ergometer.The HIIE protocol included a 5-minute warm-up at 60-70% of heart rate peak (HRp) intensity followed by 10 sets of 30 seconds above 90% with 1 minute of recovery and 3 minutes of cool down (both at the same warm-up power).MICE protocol was performed at a constant power corresponding to 60-70% of HRp and finalized at the same total work of HIIE.Blood and urine samples were collected before and after the protocols, then stored at -80°C for further analysis by the technique of Cytometric

Bead Array (CBA).The molecules measured were Tumor Necrosis Factor (TNF), Interleukin 6 (IL-6),Interleukin 8 (IL-8), Interleukin 10 (IL-10),Interleukin 12 (IL-12p70), Interleukin 1 beta (IL-1β). **Results:** We did not found any difference in the comparison of baseline levels (before both exercise protocols) of all cytokines in plasma and urine. In addition, no differences were detected in the comparison of urine and plasma levels of these molecules just after both exercise protocols. On the other hand, some changes were detected when values after exercise were compared to baseline values. Plasma levels of IL-8 significantly reduced following both protocols of exercise, although the reduction was significantly larger after MICE ($p=0.0398$). Urine levels of IL12p70 and IL-1β significantly reduced after HIIE, while both urinary concentrations of both molecules significantly increased following MICE ($p=0.0057$ and $p=0.0266$, respectively). Urine levels of TNF reduced more intensively following HIIE than after MICE ($p=0.0134$). **Conclusion:** These findings showed that both exercise protocols acutely interfere with cytokine levels. Furthermore, HIIE and MICE produced different changes in cytokine profile.

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14 - PLASMA AND URINE LEVELS OF IRISIN IN RESPONSE TO MODERATE INTENSITY CONTINUOUS AND TO HIGH INTENSITY INTERMITTENT ACUTE EXERCISES

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Keywords: Irisin, Exercise, Iso-work, Intensity

Introduction: Recently skeletal muscle has been identified as an endocrine organ due to its capacity to produce and release hormones, named “myokines”, in response

to contraction[1].Irisin, one of these myokines,has been recognized for important actionsin other sites,includingthe adipose tissue by increasing the fat metabolism in response to physical exercise[2].However, there is nodata comparing the acute effect of different intensity iso-work exercise protocols in plasma and urinary levels of irisin. Therefore, we assessed plasma and urine levels of irisin before and after high and moderate intensity iso-work protocols of physical exercise. **Methods:** Thirteen young healthy physically active men were recruited to four supervised training sessions. Two evaluation sessions were performed to measure body composition, physical activity, aerobic and anaerobic capacities before High Intensity Interval Exercise (HIIE) and Moderated Intensity Continuous Exercise (MICE) iso work exercise sessions on a cycle ergometer. The HIIE protocol invcluded a 5-minute warm-up at 60-70% of heart rate peak (HRp) intensity followed by 10 sets of 30 seconds above 90% with 1 minute of recovery and 3 minutes of cool down (both at the same warm-up power). MICE protocol was performed at a constant power corresponding to 60-70% of HRp and finalized at the same total work of HIIE. Blood and urine samples were collected before and after the protocols, then stored at -80°C for further analysis of irisin concentrations byenzyme-linked immunoassay (ELISA). **Results:** We did not found any difference in the comparison of baseline levels (before both exercise protocols) of all cytokines in plasma and urine. In addition, no differences were detected in the comparison of urine and plasma levels of these molecules just after both exercise protocols.On the other hand, the ratio between levels of irisin after exercise session and baseline levels inversely correlated with the peak of maximum volume of oxygen (VO2)only in HIIE (r=-0.675, p=0.032). **Conclusion:** Our study suggests that a better aerobic capacity mayimpair the release of irisin immediately after exercise, probably due to physiological adaptation. Furthermore, this study did not detect acute release of irisin after both exercise protocols. Maybe repeated measurements of irisin at different time-points following each exercise protocol may be necessary to show the release of this molecule, as reported by Tsuchiya et al[3].

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15 - THE ROLE OF INFLAMMATION IN PHYSICAL TRAINING INDUCED SKELETAL MUSCLE REMODELING: THE REACTIVE OXYGEN SPECIES (ROS) PARTICIPATION

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Keywords: Exercise, physical training, inflammation, ROS production.

Exercise is known by some types of activity including sports and conditioning associated with planned, structured and repetitive movement of skeletal muscle and energy expenditure. Exercise is represented by a potential homeostasis disruption by muscle activity and exercise training has been known to bring about multiple benefits to human health and sport performance, and their maintenance and/or improvement. However, it has been shown that physical exercise induces skeletal muscle damage leading to low-grade local inflammatory response. The inflammation response in skeletal muscle after exercise is still poorly known. Our hypothesis is that inflammatory response may contribute to remodeling and performance improvement of skeletal muscle. Previous data from our group showed that fatiguing exercise might cause ROS dependent neutrophil accumulation in quadriceps muscle. However, the role of neutrophil accumulation and ROS production to skeletal muscle remodeling following chronic exercise are still unknown. Thus, the aim of this study is to evaluate the role of exercise induced inflammatory response in the remodeling of skeletal muscle tissue. **Methods**: C57 mice or Gp91phox deficient were accustomed to a treadmil exercise. After that, the maximal speed capacity was measured by a progressive running until fatigue test (PFT). After 3 days, the animals were submitted

to a continuous running until fatigue test (CFT) to evaluate the maximal running capacity. Following that, the animals were divided in 4 groups non-trained wild type (nt-wt) and Gp91phox$^{-/-}$ (nt-ko) and trained wild-type (t-wt) and Gp91phox$^{-/-}$ (t-ko), that latter performed 4 weeks of training which included five exercise sessions per week, where the exercise intensity and duration were manipulated based on CFT. 3 days after the end of the training, a second CFT was carried out, which was followed by intravital microscopy of the rectus femoris muscle analysis 18 hours later. **Results:** Here, the physical training was able to increase the animals exercise workload. Interestingly, the trained gp91phox knockout workload was also higher than the trained wild-type workload. Our results also show that the number of rolling cells in the muscle vascular endothelium in trained wild-type mice was higher than non-trained 18 hours after CFT. However, there was no significant difference when compared the gp91phox knockout trained and non-trained groups. **Conclusion:** These data suggest that the leucocyte-endothelium interaction induced by exercise is workload dependent, but this relation is disrupted by ROS production deficiency.

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16 - EXERCISE TRAINING-INDUCED CHANGES IN INFLAMMATORY MEDIATORS AND HEAT SHOCK PROTEINS IN CANOEISTS

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Key words: inflammation, cytokines, HSP27, HSP70, muscle damage

Introduction. According to cytokine overtraining theory, skeletal muscle injuries are related to systemic inflammatory reaction. In response to inflammation, cells rapidly produce a series of proteins known as heat shock proteins (HSPs). These are considered to be molecular chaperones which play a universal role in maintaining cellular homeostasis. Among the subset of stress-responsive proteins, HSP27 and HSP70 are considered to be a new approach to monitoring exercise training and adaptive mechanisms [Banfi et al. 2006; Noble et al. 2008]. The study was designed to demonstrate the effect of sport training on changes in pro-inflammatory cytokines and HSPs, and their relation with muscle damage and body composition.

Materials and Methods. Six elite canoeists (19.8 ±2.9 yr) were observed during preparatory training period (March) at the 1st, the 4th and after 7 days of the conditioning camp, and then after 3 days of recovery.

Results. The canoeing training did not induce muscle damage, decreased in IL-1β and HSP27, increased in TNFα and HSP70 concentrations. The highest changes in TNFα and HSP70 were observed 3 days after conditioning camp (during recovery) compared to initial level (the 1st day of conditioning camp). TNFα correlated with HSP27 ($r = –0.563$; $P<0.01$) and HSP70 ($r = 0.651$; $P<0.001$). Any significant changes in body composition were not observed.

Conclusion. These results show that 7-day canoeing training modulates pro-inflammatory response which is related to HSPs release into the circulation, and reveal that skeletal muscle damage is not necessary to induce training-induced inflammation.

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17 - ACUTE AND CHRONIC IL-6 RESPONSES DURING FULL SEASON TRAINING IN YOUNG SWIMMERS

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Keywords: IL-6, acute effect, chronic effect, swimming training

It is well established that strenuous prolonged exercise suppresses various aspects of immune function, while excessive exercise not accompanied by sufficient rest periods may induce a chronic, low-level systemic inflammation. This exercise-induced negative effects can be counteracted by the production of anti-inflammatory cytokines, among which interleukin (IL)-6 has a dominant role. Swimming training is very hard and may lead to chronic fatigue syndrome associated with immunosuppression. This study was undertaken to investigate the acute and chronic effects of a full season swimming training on serum IL-6 both at rest and after maximal exercise testing in young swimmers. Twelve well-trained male swimmers (14.08±1.0 yrs) participated in the study. Measurements were carried out at the beginning of the training season (T1) and pre and post the taper of each of the two competitive periods (i.e., T2, T3 for the first macrocycle, and T4, T5 for the second macrocycle, respectively). At each of the above time points, blood samples were collected pre and 1 hour post a maximal, 400m swimming testing. Serum IL-6 levels were measured by ELISA using a commercially available kit and adjustment for plasma volume changes were performed before data analysis. Significant pre-post testing differences were found at T1 ($p = 0.005$) and T2 ($p = 0.005$). There were no significant differences among the post testing values throughout the experimental period, although there was a tendency for IL-6 to increase over time. Rest IL-6 values

were significantly different only between T2 and T5 (p = 0.040), although there was also a tendency for the rest values to increase from T2 to T5, while at T1 and T2 they were similar. These findings indicate that acute (pre-post testing) IL-6 responses are greater during the first swimming training macrocycle, while prolonged training may activate an adaptive mechanism which attenuates the magnitude of these responses. Interestingly, long-term training induces an increase in rest serum IL-6. Our findings appear to confirm the notion that IL-6 is a double-edged sword, exhibiting a biphasic, training-induced pattern with large, acute systemic elevations post-exercise and chronic, low-grade increases during long-term exercise training.

Special thanks go to the swimmers and Drs L.Margeti and S. Kotroni.

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18 - EFFECT OF PROBIOTICS SUPPLEMENTATION ON FUNCTION OF MONOCYTES AND URTI AFTER MARATHON

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Keywords: Exercise, Immune System, Probioticis Supplementation, Immunosuppression.

The performance of strenuous physical exercise induces acute physiological and biochemical responses with several immunosuppressant capacities. Probiotic supplementation is an attempt to mitigate the inflammatory effects of exhaustive exercise on the innate immune system. Thus, the objective of this study was to verify

the effects of probiotics supplementation on the cytokines production and the incidence of Upper Respiratory Tract Infections after marathon race. Fourteen runners were supplemented during thirty days (2.0 g/day of Lactobacillus Acidophilus, Lactobacillus Casei, Lactobacillus Lactis, Bifidobacterium Lactis e Bifidobacterium Bifidum 109 CFU or 2.0 g/day of corn starch). Posteriorly, they ran a marathon (42,195 m). Before the race, immediately after the exercise and 1 hour after exercise, 30 ml of blood were collected for determination of cellular function and plasma cytokine dosages. A questionnaire was applied about URTS during seven days after the strenuous exercise. The normality of the data was checked using the Shapiro-Wilk¡¯s test and for statistical analysis we used the repeated measures Anova Two Way, with Post-Hoc Fisher¡¯s LSD. The level of significance was p ¡Ü 5%. In our results, the production of cytokines stimulated with LPS in the placebo group had increase of IL-6 ($p < 0.05$) after the race and significant decrease of TNF-alpha ($p < 0.05$), not being watched modifications in the levels of IL-1 and IL-10. In the probiotic group were not found differences on the levels of IL-1, IL-6 and TNF-alpha, however, the results point to an increase in the production of IL-10 after the Marathon ($p < 0.05$). In plasma levels were not found significant differences in both groups at concentrations of IL-2, IL-4 and IL-6. However, in the placebo group was observed increase of IL-10 ($p < 0.05$) and in the probiotic group TNF-alpha increase after a Marathon ($p < 0.05$). Moreover, the supplementation of probiotics is associated with a smaller amount of upper respiratory tract symptoms and severity when compared with the placebo group ($p < 0.05$), besides presenting a shorter recovery and a lower percentage (¡ý 28,58%) of incidences of opportunistic infections. These results demonstrate that the marathon race generates a transient immunosuppression. It was evidenced in the placebo group that strenuous exercise affects the innate immune system. This dysfunction can therefore increase the risk of opportunistic infections in the upper respiratory tract. However, supplementation with probiotics during 30 days preserved the response of monocytes and decrease the incidence of opportunistic infections in athletes after the marathon race, being possible strategy to minimize the effects caused by exhaustive exercise on the immune system.

19 - LIFELONG TRAINING HELPS MAINTAINING CD4 AND CD8 NAÏVE T-CELLS WHILE REDUCING THE NUMBER OF SENESCENT NAÏVE T CELLS

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Keywords: Immunosenescence; master athletes; lifelong training; naïve; lymphocytes T.

Background: Some of the characteristics of immunosenescence in the T-cell pool, include low numbers and proportions of naïve T-cells, specially $CD8^+$ T-cells, and a large number of memory T-cells, mainly $CD8^+$ T-cells in late stage of differentiation. However, it has been suggested that chronic exercise can have an ´´anti´´ immunosenescence effect by maintaining/increasing the number of naïve T-cells. **Purpose:** The aim of this study was to evaluate the effect of lifelong training on senescence and percentage of naive T-lymphocytes in response to acute exercise. **Material and Methods:** Nineteen master athletes who regularly participated in training and competitions for more than 20 years and a control group of 9 healthy individuals participated in this study. All subjects performed a progressive test to exhaustion on a cycle ergometer. Blood samples were obtained before (Pre), 10 min after the test (Post) and 1 h after the test (1h). The phenotypic study of peripheral blood T-cells was performed by flow cytometry. Expression genes of interest were done on naïve T-cells purified by cell sorting. For the analyses of change, accounting for the multilevel design of the study, hierarchical random effects models (REM) were constructed using a multilevel modeling approach. **Results:** We observed a negative influence of age on naïve $CD8^+$ T-cells and a positive effect of VO_{2max} on naïve $CD4^+$ T-cells (-0.5964±0.2192 and 0.0599±0.0024, respectively). This suggests that the effect of age is greater than training on naïve $CD8^+$ T-cells, whereas individuals with a better physical condition (higher VO_{2max} values) tend to have a higher number of naïve $CD4^+$ T-cells. Master athletes showed lower percentages of senescent $CD4^+$ (-

5.8145±2.4227) and $CD8^+$ (-13.0661±4.9568) T-cells including lower percentage of senescent naïve $CD4^+$ and $CD8^+$ T-cells (-5.3182±2.5761 and -9.3624±2.0992, respectively). The mRNA expression of the CCR7 gene for naïve $CD8^+$ T-cells was not different between masters and controls and did not change in response to the maximal protocol test. **Conclusion:** Maintaining high levels of aerobic fitness during the natural course of aging may help prevent the accumulation of senescent T-cells while maintaining an adequate number of naïve T-cells and preserving the immune system ability to recognize and respond to new pathogens with ageing.

20 - REACTIVATION OF EPSTEIN-BARR VIRUS FOLLOWING PROLONGED CYCLING.

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Epstein-Barr Virus (EBV) is a herpes virus that typically infects 80-90% of adults, establishing lifelong latent infection in epithelial cells and B-lymphocytes in the oropharynx. Under significant physical and/or psychological stress the immune system's ability to keep EBV latent may be lost and reactivation may occur so EBV DNA appearance in saliva (in carriers) may serve as an *in vivo* marker of immune status. Prolonged exercise can cause a transient immune depression for up to 24 h post exercise (Walsh et al. 2011). However it is currently unknown what effect this has on the control and subsequent reactivation of EBV in the hours following exercise. The objective of this study was to investigate the acute effect of prolonged cycling on EBV reactivation and other immune markers in blood and saliva up to 44 h post exercise. Following ethics approval, eight trained male cyclists (mean ± SD) age 31 ± 8 yrs, VO_2max 58.7 ± 9.0 $ml \cdot kg^{-1} \cdot min^{-1}$ volunteered to take part. In a randomised design, after an overnight fast participants cycled at 20%D or rested for 2.5 h. Unstimulated saliva samples were provided upon waking on the morning of

each trial as well as the two following mornings. Unstimulated saliva and venous blood samples were collected immediately pre, post, and 1 h post exercise/rest. EBV DNA was measured using quantitative polymerase chain reaction (qPCR). EBV serology and salivary immunoglobulin A (s-IgA) were determined by ELISA. Venous blood samples were analysed for white blood cell counts. All eight participants were EBV seropositive and EBV DNA was detected in saliva of three participants during the study period. A pre-to-post-exercise increase in EBV viral load was evident in two of these typically occurring at 20-44 h post-exercise (with an average 10-fold increase in EBV viral load). Neutrophil cell counts significantly increased pre-to-post-exercise (1.8 ± 0.8 to 7.8 ± 2.7 x 10^9/L, P<0.05) and remained elevated at 1 h post (9.0 ± 2.6 x 10^9/L, P<0.05). s-IgA concentration significantly decreased from waking to post and 1 h post-exercise (P<0.05). s-IgA concentration and secretion rate significantly increased from post and 1 h post to 20 and 44 h post-exercise (P<0.05). No post-exercise increase in EBV DNA was detected in saliva for the majority of subjects (75%) and for those who did experience an increase it typically peaked 20-44 h post-exercise. There was evidence of a significant stress response to the exercise (e.g. cell trafficking and s-IgA) so perhaps a more strenuous (or prolonged) exercise bout would result in greater changes in EBV viral load, however this requires further research. Further exploration of the time period between 1 h and 20 h post-exercise would also be valuable.

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21 - MUCOSAL IMMUNE MARKERS IN PROFESSIONAL ENGLISH FOOTBALL PLAYERS.

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Team sport athletes appear to be more susceptible than normal to infection, especially upper respiratory tract infections (URTI) (i.e. coughs, sore throat, runny nose etc), during periods of intensified training and match play (Cunniffe et al. 2011). A decrease in individual relative concentration of salivary immunoglobulin A (s-IgA) has been shown to be associated with an increased risk of URTI (Neville et al. 2008). The objective was to examine the relationship between s-IgA and upper respiratory illness during a period of intensive match play (fixtures) in a group of professional English football players. Following University ethics approval, 16 male footballers from a professional English League 1 club provided unstimulated saliva samples on the same morning of each week for 16 weeks. Upper respiratory illness symptoms were recorded on a questionnaire. Saliva samples were analysed for s-IgA concentration and secretion rate. Individual healthy baseline s-IgA was calculated as the average across all weeks when no illness symptoms were present. Data are expressed as mean ± SEM. Over the 16-week study period, 238 saliva samples were collected and analysed. Mean s-IgA concentration was 127 ± 5 $mg{\cdot}L^{-1}$ with a mean CV of 53%, between individuals CV was 62%. Mean s-IgA secretion rate was 60 ± 1 $mg{\cdot}min^{-1}$ with a mean CV of 57%, between CV was 69%. Two individual illness episodes occurred during the 16-week period, both when s-IgA was lower than 40% individual healthy baseline, with symptoms lasting 4–7 days. s-IgA concentration and secretion rate were highly variable within and between individuals. s-IgA decreased following a period of intensified competitive match play to 40-70% of each individual players´ healthy baseline. A decrease in s-IgA below 40% of healthy baseline would suggest an increased risk of infection however not all periods of low s-IgA resulted in illness symptoms. Furthermore, just two illness episodes occurring during the monitoring period so it is not possible to confirm a link between s-IgA values (as absolute values or % of healthy baseline) and illness incidence. Whole squad s-IgA increased as the number of days between competitive matches increased (i.e. no midweek matches). Based on these results coaching staff could consider the amount of recovery time given to players during intensified periods as factors such as time spent travelling, and disruption to sleep and nutritional routines alongside increased competitive workload may be responsible for suppression of immunity.

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22 - THE COMPARISON EFFECT OF OVERTRAINING AND OVERTRAINING PLUS VIT D3 ON MIR181B AND INFLAMMATORY FACTORS IN WISTAR RATS

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Nuclear factor κB (NF-κB) activation contributes to EC activation and dysfunction, which play critical roles during the development of atherosclerosis [1]. In the arterial endothelium, NF-κB signaling is activated by many risk factors for atherosclerosis, including inflammatory cytokines, diabetes, oxidized LDL, angiotensin II, and hemodynamic forces. The resulting NF-κB signaling leads to the expression of proinflammatory genes, including cytokines, adhesion molecules, and chemokines [2]. We recently identified miR-181b as a critical regulator of NF-κB-mediated vascular inflammation by virtue of miR-181b's ability to directly target importin-α3, a protein critical for NF-κB translocation from the cytoplasm to the nucleus [3]. With use of a microarray profiling approach, miR-181b expression was rapidly reduced in response to the proinflammatory stimulus TNF-α. Both TNF-α and lipopolysaccharide reduced miR-181b expression in ECs in vitro and in the aortic intima in vivo [3]. Gain-of-function and loss-of-function studies revealed that miR-181b regulated the NF-κB signaling pathway and NF-κB-responsive gene expression in the activated vascular endothelium. Consistent with its inhibitory effect on NF-κB activation, systemic

delivery of miR-181b mimics reduced EC activation, leukocyte accumulation, and lung inflammation and improved survival by approximately 50%. In contrast, miR-181b inhibition exacerbated inflammation and increased NF-κB-responsive gene expression. [4]. In this study 30 rats selected and divided to 3 groups control, overtraining +D3 and overtraining exercise. Overtraining protocol was done with speed 15 m/min in first week and 25 m/min in last week. All protocol training was for 12 weeks. Speleenectomy where done training protocol, and Eliza method used to NF-κB and TNF-a and ICAM-1. The results of this study showed a increase in the amount mir181b of decrease in the levels of NF-κB and TNF-a and ICAM-1 in overtraining +D3 group that difference was significant (p=0.01). The results also showed increase in levels of NF-κB and TNF-a and ICAM-1and decrease in mir181b in overtraining group difference was significant (p=0.01). Based on the results of this research, it can be concluded that overtraining+D3 group lead decrease inflammatory factors in contrast with overtraining group.

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23 - THE EFFECT OF CRANBERRY ON LEVELS OF INFLAMMATORY AND ANTI- INFLAMMATORY PLASMA CYTOKINES DURING 10-WEEK OF INTENSIVE TREADMILL TRAINING IN ENDURANC

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Keywords: cranberry, intensity training, inflammatory, anti- inflammatory

Inflammation is a response of the innate immune system, and is the reaction of the body to various stresses including cellular damage or infection caused by physical and/or chemical agents.The inflammatory response includes release of various soluble molecules called cytokines and chemokines, which mediate interactions between cells, thus affecting processes such as immunity and protein synthesis. [1]. As these inflammatory markers accumulate, they facilitate the infiltration and activation of neutrophils, macrophages, and lymphocytes which are needed to destroy and remove pathogens and damaged tissue. Innate immunity provides the body with a very rapid first line of defense. [2]

Quercetin was reported as a long lasting anti-inflammatory substance that possesses strong anti-inflammatory capacities [3]. It possesses anti-inflammatory potential that can be expressed on different cell types, both in animal and human models [3]. It can also play a modulating, biphasic and regulatory action on inflammation and immunity. Additionally, quercetin has an immunosuppressive effect on dendritic cells function [4].

The purpose of this study was to determine the effects cranberry on levels of plasma cytokines during 10 weeks of treadmill training in endurance-trained athletes Twenty male endurance-trained athletes (age 20 years, weight 75 kg) participated in this study. The participants were randomly assigned to exercise supplement (E+S, n=10), and exercise control (EC, n=10) groups. All subjects participated in 10 weeks of intensive treadmill training. Venous blood samples were collected immediately after exercise (T1), 1 hour after exercise (T2) and 24 hours after exercise (T3). In the EC group, 10 weeks of training increased the seminal, IL-6, Tumor necrosis factor alpha (TNF- α) immediately after exercise (T1) , 1 h after exercise (T2), 24 hours after exercise (T3)($P<0.05$). However, E+S group showed significant decrease in TNF- α and IL-6 with a corresponding increase in IL1ra immediately after exercise (T1), 1 h after exercise (T2) and 24 hours after exercise (T3) $p<0.05$. it="" is="" proposed="" that="" cranberry="" decreases="" inflammatory="" cytokine="" such="" as="" il-6="" and="" tnf="" a="" corresponding="" increase="" in="" anti-inflammatory="" il1ra=""

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24 - THE COMPARISON OF ENDURANCE TRAINING WITH MODERATE INTENSITY AND OVERTRAINING ON TH1/TH2 BALANCE IN WISTAR MALE RATS

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Type 1 (T1) and Type 2 (T2) lymphocytes promote cell-mediated immunity and humoral immunity respectively (1). Evidence accumulated over the past two decades has demonstrated diverse responses of T1 and T2 cells to acute exercise or longterm training at moderate and high intensities (2). The potential of using the T1/T2
balance as an indicator of immune function changes in response to exercise is discussed (3). This study is about effects of endurance training with moderate intensity and overtraining on balance these two cytokines. In this study 30 rats selected and divided to 3 groups control, moderate and overtraining exercise. Moderate training protocol was done for 12 weeks with speed 30 m/min in first week and 23m/min in last week. Overtraining protocol was done with speed 15 m/min in

first week and 25 m/min in last week. All protocol of training was for 12 weeks. Speleenectomy where done after training protocol, and Eliza method used to, Interleukin 4 (IL4) and Interferon γ (IFNγ). The results of this study showed a increase in the amount of (IFNγ) and decrease in the levels of IL4 in moderate training group that difference was significant (p=0.01). The results also showed increase in levels of IL4 and decrease IFNγ levels in overtraining group difference was significant (p=0.01). Based on the results of this research, it can be concluded that doing moderate training lead to increase IFNγ and overtraining case to increase IL4.

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25 - THE COMPARISON EFFECT OF OVERTRAINING AND OVERTRAINING PLUS VIT D3 ON CYTOKINE KINETICS IN WISTAR RATS

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Keywords: Overtraining, Vit D3, IFNγ, IL4

It has been reported that moderate or intermittent exercise enhances immune function but overtraining cause numerous changes in immunity, which possibly reflects physiological stress and suppression (1). Athletes tolerating more intense

levels of training may be at increased risk of upper respiratory tract infection (URTI) during periods of sever exercise and for the few weeks after race events. Interestingly, most of the studies used applied voluntary exercise, even though the effects of enforced physical exercise, especially with different loads, are unclear. There is little information regarding whether regular exercise above a certain intensity or duration could be harmful (2).

However, with overtraining, which is still a poorly understood process, the homeostatic balance involving a wide range of hormonal, metabolic, and immunologic factors is altered. Vitamin D is known to have important effects on both innate and adaptive immune function with implications for host defence. The studies that have reported modulation of pro- and antiinflammatory cytokine production by vitamin D have generally administered 1, 25(OH)2D in vivo in animals (3) or in vitro in human peripheral blood mononuclear cell cultures and observed increases in anti-inflammatory cytokines such as transforming growth factor-β, IL-4 and IL-10 and reductions in pro-inflammatory cytokines including IL-2, IL-6, IFN-γ and TNF-α(4)..In this study 30 rats selected and divided to 3 groups control, overtraining +D3 and overtraining exercise. Overtraining protocol was done with speed 15 m/min in first week and 25 m/min in last week. All protocol of training was for 12 weeks. Speleenectomy where done training protocol, and Eliza method used to, Interleukin 4 (IL4) and Interferon γ (IFNγ). The results of this study showed a increase in the amount of (IFNγ) and decrease in the levels of IL4 in overtraining +D3 group that difference was significant (p=0.01). The results also showed increase in levels of IL4 and decrease IFNγ levels in overtraining group difference was significant (p=0.01). Based on the results of this research, it can be concluded that doing overtraining+D3 lead to increase IFNγ and overtraining case to increase IL4.

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26 - ANTIINFLAMATORY EFFECTS OF EXERCISE TRAINING IN ANIMALS EXPOSED TO DIESEL EXHAUSTED PARTICLES

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Keywords: pollution, exercise training, animal model.

Air pollution has been recognized as a health hazard worldwide and responsible to increase in morbidity and mortality around world, although mechanism that it causes adverse health effects are not properly understood. Studies have demonstrated that diesel exhaust particulates (DEP) increase airway inflammation and can exacerbate some diseases. In other hand, moderate exercise training have been recognized as an important stimulator of immune system with anti-inflammatory effects. In this way, our aim is to evaluate if moderate aerobic exercise training prior to exposure to DEP alter the inflammatory profile and lung mechanics in a mouse model. **Methods**: 40 BALB/C mice were divided in 4 groups: sedentary (S); exercise training (T); Pollution (P); exercise training + pollution (TP). Animals were submitted to exercise training protocol during 4 weeks (5x/wk; during 1h). After that, animals remained training but also beginning to be exposed to diesel exhaust particles (DEP) (5x/w; during 1h), during 6 weeks. 48hs after last session of training and exposure particles, animals were anesthetized and euthanized to evaluate airway responsiveness to increase concentrations of aerolized methacholine, bronchoalveolar lavage (BALF) and cytokines in lung homogenate. **Results**: We found an increasing total number of

inflammatory cells (p<0.02), macrophage cells (p<0.05) and neutrophils (p<0.001) in BALF as well as increase in inflammatory cytokines: IL-12p40 (p<0.05) and IL-23 (P<0.001) in P group compared to other groups. Exercise training were effective in reduce these inflammatory parameters in TP group compared to P group. In evaluation of airway responsiveness, we found an increase in resistance of respiratory system in groups that were submitted to exercise training compared to groups that remained sedentary (S and P groups), although in evaluation of elastance of respiratory system, we found an decrease in groups P and TP groups compared S and T group. **Conclusion**: Moderate aerobic exercise training prior to exposure to DEP seems to be effective in reduce lung inflammation although cannot prevents the worsening in mechanical of respiratory system.

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27 - EFFECT OF STRENGTH TRAINING SESSION ON IMMUNOLOGICAL AND PHYSIOLOGICAL BLOOD MARKERS

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Keywords: physical exercise, immune function, leukocytes.

The strength exercises are considered an essential part of any kind of training program, and skeletal muscle hypertrophy is one of the main adaptations to this type of training. Although widely studied, the mechanisms responsible for this adaptation are not completely clear, moreover, little is known about the inflammatory responses in strength training with durations of muscle actions predominantly eccentric. Hypertrophy of muscle tissue is an important phenomenon in high performance sport, for recreational practitioners of physical activity in the aging process and also pathological conditions such as obesity, AIDS, muscular dystrophy and diabetes. The aim of this study was to evaluate the immune response induced by strength training protocol with muscle actions predominantly eccentric. Twenty volunteers 10 sedentary and 10 regular weight training practitioners participated in this study (height 1.73 ± 0.06 m trained and 1.75 ± 0.08 m untrained; and weight 74.78 ± 14.91 kg trained and 73.05 ± 3.40 kg untrained). They hold 4 sets of 8-10 reps of exercise (leg press, extensor bench and leg curl), 65% of 1RM, 90s range, and the duration of the execution of each repetition 2” to concentric and 3” to eccentric actions. Blood samples were collected immediately before, after, 2 and 24 hours of the final training session. Here we investigated physiological mediators (lactate) and subpopulation of leukocytes (neutrophils, lymphocytes and monocytes). The training session was able to increase lactate levels immediately after the end of exercise (1.79 ± 0.85 to 9.98 ± 4.87) and return to baseline (3.19 ± 1.81) 2 hours later. Comparing groups only the neutrophil values presented significant differences. In comparison between times in each group, for the neutrophil values, the sedentary group had higher values in the time of 2 hours after exercise (8.04 ± 3.92), while the regular weight training practitioners presented higher values in the time of 2 hours after (4.69 ± 2.07) compared to the pre and 24 hours (2.79 ± 1.49 / 2.97 ± 1.32). For the monocyte concentrations, the sedentary group presented higher values only in the time of 2 hours (0.74 ± 0.33) and the regular weight training practitioners only in the post exercise period (0.78 ± 0.30). For the lymphocyte concentrations in the sedentary group there was a reduction 2 hours after (2.31 ± 0.57 to 1.42 ± 0.36), whereas in the

regular weight training practitioners there was an increase only in post-training values (2.77 ± 0,74). The results show that strength training session is able to induce changes in the subpopulations of leukocytes, and provokes significant, although transient, modulation of the immune system, specifically of the leukocyte sub-population.

28 - CHANGES IN THE IMMUNE RESPONSE DURING AN ATHLETICS TRAINING AND COMPETITION SEASON IN 800 M HIGH-LEVEL ATHLETES

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Introduction: White blood cells are an important part of the immune system, playing a role in defense against disease agents. The immune system may be affected by the level of activity in which an athlete is engaged (Vleck et al., 2014). Through several mechanisms, the immune system may be depressed during intense endurance activity, resulting in an increased risk of illness or infection (Knez et al., 2006). The aim of this study was to analyze the changes in the immune response during a complete athletics season in 800 m high-level athletes.

Methods: Thirteen male athletes of national and international level in 800 m (personal best ranging from 1:43 to 1:58 min:ss) participated in this study (age: 22.9 ± 5.3 years; height: 175.2 ± 5.5 cm; body mass: 62.9 ± 4.4 kg). A total of 3 blood samples tests (T1, T2, T3) were taken from October to June, every 4 months. The participants were asked to rest from training the day before the sampling. Before blood sampling the athletes rested on a bed for at least 10 minutes. Blood samples were taken from the athlete in supine position from the antecubital vein by a qualified laboratory technician using the Vacuette system and collected in tubes containing EDTA K 3 (3 ml). White blood cells (WBC), neutrophils, lymphocytes, monocytes, eosinophils, basophils, platelets and mean platelet volumen (MPV) counts were measured using hematology analyzer XN-9000 (Roche Diagnostics, USA). One-way

ANOVA and post-hoc Bonferroni method with significance level of 5%, were used for data analysis.

Results: Significant decreases in WBC ($P < 0.05$), neutrophils ($P < 0.05$), and monocytes ($P < 0.05$) were observed from T2 to T3. Significant increases occurred in MPV ($P < 0.05$) from T1 to T3, and from T2 to T3. The rest of the parameters analyzed did not show significant variations.

Conclusion: Significant decreases occurred in WBC, neutrophils, and monocytes from T3 to T5, suggesting a depression of the immune system at the end of the season. This finding is in line with Horn et al. (2010), who observed a decreased number of monocytes and WBC in triathletes. This depressed response observed in our study could be due to the more intense and specialized exercises performed during the summer competition period (from T2 to T3), and could increase the risk of illness or infection. Besides, the significant increase of MPV is consistent with the well-established evidence that aerobic physical activity is effective to enhance circulating activated platelets (Whittaker et al., 2013). Therefore, monitoring the immune response in athletes may help coaches and athletes to optimize the regulation of training contents and may be useful to diagnose states of overreaching or overtraining in athletes.

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29 - THE EFFECT OF CHLORELLA PYRENOIDOSA SUPPLEMENTATION ON IMMUNE RESPONSES TO TWO DAYS OF INTENSIFIED TRAINING

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Keywords:

Introduction The aim of this study was to investigate the effects of supplementation with the freshwater single-celled microalgae *Chlorella Pyrenoidosa* (Chlorella) on sIgA responses to two days of intensified training.

Methods Twenty-two trained males and 4 females (age 29.1 ± 8.7 years; VO_{2max} 53.7 ± 11.7 ml.kg.min^{-1}) took part in the study. Resting unstimulated saliva samples were collected at baseline (week-0) and following 4, 5, and 6 weeks (weeks-4, -5, -6) of daily supplementation with either placebo (PLA) or Chlorella (SunChloralla A tablets, 30/day: equivalent to 6 g/day of Chlorella). During week-4 subjects undertook a 2-day intensified training period (2 sessions per day on a cycle ergometer: day 1 morning, VO_{2max} test; afternoon: high-intensity interval training (HIT) consisting of 3 x 30 sec Wingate sprints with 90 sec recovery intervals; day 2 morning, 90 minutes at 25%Δ(~60% VO_{2max}), afternoon; 3 x 30 sec HIT). Saliva samples were also collected pre-, post- and 1 h post exercise bouts for determination of secretory IgA (sIgA) by ELISA.

Results Only significant main effects are reported here (for 2-way mixed ANOVA only interactions are reported). All other comparisons/analyses were non-significant ($P > 0.05$).

Resting sIgA For sIgA concentration a significant trial × time interaction was seen ($P = 0.024$) with [sIgA] tending to increase with Chlorella by week-5 and week-6 (*post hoc* $P = 0.078$ and 0.056, respectively) but remaining unchanged in PLA (PLA vs Chlorella: week-0, 205 ± 106 vs 192 ± 80; week-4 = 176 ± 90 vs 199 ± 86; week-5 = 185 ± 103 vs 260 ± 112; week-6 = 192 ± 57 vs 368 ± 261).

For sIgA secretion rate a significant trial × time interaction was seen ($P = 0.016$) due to an increase with Chlorella at week-4, week-5 and week-6 ($P = 0.020$, < 0.001, and 0.016) whilst it remained unchanged in PLA (PLA vs Chlorella: week-0 = 54 ± 33 vs 57 ± 37; week-4 = 54 ± 35 vs 83 ± 57; week-5 = 63 ± 46 vs 98 ± 47; week-6 = 58 ± 35 vs 85 ± 59).

Responses to exercise For sIgA secretion rate there was a significant trial × time interaction for exercise bouts 2 ($P = 0.016$) and 3 ($P = 0.017$). For bout 2 there was no change in PLA ($P = 0.075$) but a significant increase with Chlorella at pre-exercise (i.e. week-0 = 57 ± 37 vs pre-exercise = 100 ± 82, $P = 0.009$) and post-exercise (93 ± 97, $P = 0.010$). For exercise bout 3 there was no change in PLA ($P = 0.996$) but a significant increase with Chlorella at pre-exercise (88 ± 50, $P = 0.023$), post-exercise (77 ± 41, $P = 0.005$) and 1h post-exercise (87 ± 43, $P = 0.004$).

Conclusion Supplementation with 6 g/day Chlorella for 4 weeks has beneficial effects on resting sIgA, which might be beneficial during periods of intensified training. However, the present findings suggest it is possible that a longer pre-training supplementation period (e.g. 6-8 weeks supplementation) is required for optimal benefit.

30 - ACUTE AND CHRONIC SYSTEMIC IRISIN RESPONSES DURING FULL SEASON TRAINING IN YOUNG SWIMMERS

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Keywords: Irisin, acute effect, chronic effect, swimming training

Regular physical activity entails important fitness benefits and combats the development of common diseases such as obesity and type 2 diabetes. More specifically, systemic effects of exercise such as the increase in total energy expenditure can be attributed to a messenger system between muscle and fat tissue. That system includes irisin, a protein which is secreted into the bloodstream and triggers the browning of white adipose tissue. There are contradictory findings concerning the influence of exercise training on serum irisin concentration. This study was undertaken to investigate the acute and chronic effects of a full season swimming training on serum irisin, both at rest (PRE) and after (POST) maximal exercise testing in young volunteers. Twelve well-trained male swimmers (age 14.08±1.0 yrs) participated in the study. Measurements were carried out at the beginning of the training season (T1) and pre and post the taper of each of the two competitive periods (i.e., T2, T3 for the first macrocycle, and T4, T5 for the second macrocycle, respectively). At each of the above time points, blood samples were collected pre and 1 hour post a maximal, 400m swimming testing. Serum irisin levels

were measured by ELISA using a commercially available kit and adjustment for plasma volume changes were performed before data analysis. Significant PRE-POST (testing) differences were found at T3 ($p = 0.039$), while all POST values were below the PRE ones throughout the experimental period. No significant differences were found between the POST values, although there was a tendency for irisin to increase at T2, T4, and T5. Moreover, rest (PRE) irisin values were not significantly different throughout the experimental period, although there was a tendency for them to decrease at T2 and T4. Our findings suggest that exercise affects circulating irisin levels, which are probably depended on the volume and intensity of exercise training. These findings might shed more light on the physiological role of irisin and support the notion that this factor links physical activity to energy metabolic homeostasis.

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31 - CYTOKINE PRODUCTION IN LPS-STIMULATED WHOLE BLOOD CULTURES FROM CONTINUOUS EXERCISES PERFORMED AT DIFFERENT INTENSITIES IN WELL-TRAINED MEN

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Keywords: Physical exercise, Metabolism, Inflammation, Health

Background: Exhaustive exercise can promote changes in inflammatory response, and lead to pro-inflammatory (higher TNF-α levels) or anti-inflammatory (higher IL-10

levels) status. The inflammatory responses can be influenced by exercise intensity, duration, and physical fitness level. However, it is unknown the better intensity to promote anti-inflammatory response in well-trained men. **Objective:** To evaluate the effects of acute exercise sessions performed at moderate, heavy, and severe intensity on cytokines responses in well-trained men. **Methods:** Seven healthy male volunteers (Age_{mean}=31±6.3; $Weight_{mean}$=79.4±13.7; BMI_{mean}=25.5±2.8) performed an incremental protocol in cycle ergometer to determine the intensities domain of rectangular tests. The moderate (90% of lactate threshold (PLac)), heavy (PLac + 50% Δ between Anaerobic threshold (PLan) and PLac), and severe (PLan + 50% Δ between maximum power output (W_{peak}) and PLan) intensity domain was performed until voluntary exhaustion or when the subject completed 1 hour of testing. Blood samples were collected at rest, immediately and 60-min after different exercise sessions. We used whole blood in short time (1h) LPS-stimulated cultures for analyses IL-6, IL-10, and TNF-α levels. For statistic treatment, the comparison between the intensities was performed by ANOVA one-way and Bonferroni post-hoc was used; for all cases we adopted p<0.05. strong="">Results: When compared the intensities, no difference was observed between them in the alterations of IL-6 and TNF-α levels; however, heavy intensity session showed a tendency to cause a greater decrease in TNF-α (Δ_{heavy}= -86.13pg/mL; F=2.953; p=0.079) when compared with moderate ($\Delta_{moderate}$=3.44pg/mL) and severe intensities (Δ_{severe}=148.55pg/mL). On the other hand, there was a significant increase in the IL-10 levels immediately after exercise sessions performed at moderate and heavy intensity, with higher values in both intensities ($\Delta_{moderate}$=11.44pg/mL; Δ_{heavy}=11.93pg/mL) when compared with severe intensity (Δ_{severe}= -6.38pg/mL; F=4.632; p=0.025); however, only the session training performed at heavy intensity was able to sustain increased IL-10 levels 60-minutes post-exercise (Δ_{heavy}=6.65pg/mL; F=5.340; p=0.016). **Conclusion:** The anti-inflammatory response promoted by acute exercise session is time and intensity-dependent in well-trained men given that, when compared the intensities, only the session exercise performed at heavy intensity was able to provide a trend of reduction in TNF-α parallel with significant increase of IL-10 concentrations.

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32 - EFFECT OF STRENGTH TRAINING SESSION ON IMMUNOLOGICAL AND PHYSIOLOGICAL BLOOD MARKERS

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Keywords: physical exercise, immune function, leukocytes

The strength exercises are considered an essential part of any kind of training program, and skeletal muscle hypertrophy is one of the main adaptations to this type of training. Although widely studied, the mechanisms responsible for this adaptation are not completely clear, moreover, little is known about the inflammatory responses in strength training with durations of muscle actions predominantly eccentric. Hypertrophy of muscle tissue is an important phenomenon in high performance sport, for recreational practitioners of physical activity in the aging process and also pathological conditions such as obesity, AIDS, muscular dystrophy and diabetes. The aim of this study was to evaluate the immune response induced by strength training protocol with muscle actions predominantly eccentric. Twenty volunteers 10 sedentary and 10 regular weight training practitioners participated in this study (height 1.73 ± 0.06 m trained and 1.75 ± 0.08 m untrained; and weight 74.78 ± 14.91 kg trained and 73.05 ± 3.40 kg untrained). They hold 4 sets of 8-10 reps of exercise (leg press, extensor bench and leg curl), 65% of 1RM, 90s range, and the duration of the execution of each repetition 2” to concentric and 3” to eccentric actions. Blood samples were collected immediately before, after, 2 and 24 hours of the final training

session. Here we investigated physiological mediators (lactate) and subpopulation of leukocytes (neutrophils, lymphocytes and monocytes). The training session was able to increase lactate levels immediately after the end of exercise (1.79 ± 0.85 to 9.98 ± 4.87) and return to baseline (3.19 ± 1.81) 2 hours later. Comparing groups only the neutrophil values presented significant differences. In comparison between times in each group, for the neutrophil values, the sedentary group had higher values in the time of 2 hours after exercise (8.04 ± 3.92), while the regular weight training practitioners presented higher values in the time of 2 hours after (4.69 ± 2.07) compared to the pre and 24 hours (2.79 ± 1.49 / 2.97 ± 1.32). For the monocyte concentrations, the sedentary group presented higher values only in the time of 2 hours (0.74 ± 0.33) and the regular weight training practitioners only in the post exercise period (0.78 ± 0.30). For the lymphocyte concentrations in the sedentary group there was a reduction 2 hours after (2.31 ± 0.57 to 1.42 ± 0.36), whereas in the regular weight training practitioners there was an increase only in post-training values (2.77 ± 0, 74). The results show that strength training session is able to induce changes in the subpopulations of leukocytes, and provokes significant, although transient, modulation of the immune system, specifically of the leukocyte sub-population.

33 - IMMUNE AND HEMATOLOGICAL CHARACTERISTICS OF 2016 OLYMPIC CHAMPION SHOOTING ATHLETE: A CASE STUDY INVESTIGATION IN TRANSITION PERIOD TRAINING

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Keywords: Immune, hematologic, shooting, athlete, shooter, transition period training

The purpose of this study was to investigate the immune and hematological characteristics of the Vietnamese shooter who won gold medal in Olympic Rio 2016. The subject is a champion in 10m air pistol (60 shots) men. He practiced 4 weeks after returning from Rio 2016 as transition period before starting a new circle training. Blood was taken in the morning before meals at the end of transition period. Blood chemistry included white blood cell (WBC), red blood cell (RBC), hemoglobin concentration (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean hemoglobin content (MCH), mean corpuscular hemoglobin content (MCHC), platelets (PLT), and testosteron hormone, cortisol hormone, metanephrine/plasma were analyzied.The results show that almost indicator were in normal range: WBC 6.37×10^9 L; PLT 208×10^9 L, Hb 17.0g/dL, Hct 47.8%, MCV 83.9fL, MCH 29.8 pg, MCHC 35.6g/dL, except RBC 5.7×10^9 L was slightly higher than normal range (3.8-5.6×10^9 L). Eventhough the athletes was 42 years old but his hormon and metabolic system were still in good condition. Compared to baseline values, testosteron 499.4ng/dL, cortisol 9.2µg/dL, adrenaline 65.0pg/ml, metanephrine/plasma 57.26pg/mL were in normal range. This results demonstrated that elite shooter have a good response in immune and metabolic system. Training hard with the stress of focus and static strength have positive effects to shooting athlete and it still maintained a good response even during the transition period.

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34 - INFLAMMATION PREDICTS PERFORMANCE IN MARATHONERS WITH EXERCISE-INDUCED BRONCHOCONSTRICTION

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Keywords: Exercise-induced bronchoconstriction; marathon runners; inflammation; performance.

Introduction: Exercise-induced bronchoconstriction (EIB) is defined as a transient narrowing of the airways that occurs after exercise[1]. The objective of this study was to investigate the role of inflammation and aerobic capacity in performance of non-professional marathon runners with and without EIB. **Methods:** Thirty-eight male amateur marathon race participants in the International Marathon of São Paulo, 2012, were recruited. The study was approved by the ethics committee on human research of the Federal University of São Paulo under the number 0573/11. All participants underwent pulmonary function testing, cardiopulmonary test and peripheral blood analysis to measure creatine phosphokinase (CPK) and high-sensitivity C-reactive protein (CRP_{HS}). **Results:** Twenty-nine athletes showed normal results in pulmonary function test and 9 subjects present a decrease higher than 10% in expiratory forced volume in first second, characterizing an EIB diagnosis.

Statistically difference was found in maximal oxygen consumption (EIB negative group mean: 47.75; EIB positive group mean: 43.91; p=0.02). No difference was observed between groups analyzing the race finishing time (EIB negative group mean: 4h 32min 34sec; EIB positive group mean: 4h 26min 34sec; p=0.74). The negative EIB group presented a negative moderate correlation between marathon finishing time and VO_{2max} (rho= -0.532 and p=0.005). There was found a significantly positive correlation between marathon finishing time and CRP_{HS} (rho=0.714; p=0.04), and between marathon finishing time and Δ CPK (rho=0.719; p=0.04), both measured immediately after the marathon, in EIB positive group. The EIB negative group did not show any correlation with biomarkers. **Discussion:** The correlation result found in EIB negative group as expected showed that the aerobic performance it's predicted by aerobic capacity[2]. The positive correlation between marathon finishing time and both CRP_{HS}, a conventional biomarker of systemic inflammation and a CPK a marker of damage tissue, shows that in EIB subjects inflammation and damage tissue influence the EIB athletes' performance[3,4]. **Conclusion:** Our results shows that inflammation and damage tissue seems to play an important role in EIB positive runners performance, and that the aerobic capacity can be used as a predictor of performance only in non-EIB subjects.

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35 - EFFECTS OF ORAL GLUTAMINE SUPPLEMENTATION ON PLASMA LYMPHOCYTES COUNT AFTER EXHAUSTIVE RESISTANCE EXERCISE

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Keywords: Glutamine, lymphocytes, resistance exercise

Plasma glutamine, decreases in patients with infection, overtrained athletes and after prolonged and intense aerobic exercise[1]. This is accompanied by a transient post exercise drop in lymphocytes count. Restoration to normal levels appears to be faster or is not affected after previous glutamine administration[2]. During dynamic resistance exercise, however, the physiological requirements may differ from those observed during aerobic effort. Thus our study aimed to examine the acute effects of glutamine supplementation after exhaustive resistance exercise. Ten physically active males (age: 21.4±0.11yrs), able to squat against a weight at least 150% of their body mass, participated in the study. Following a controlled diet and physical activity, participants were administered either 0.1gr L-glutamine·kg^{-1} diluted in 250ml water (GLN condition-GC) or 250ml water (Control Condition-CC) fifteen days apart, before the execution of a resistance exercise protocol using a double blind and counter balanced design. Resistance exercise involved the execution of multiple sets (until exhaustion) of fifteen repetitions back squats (90° knee flexion) with a load 65% of 1RM, constant paced at 30 reps·min^{-1}, with 1min of rest between sets. Blood samples were obtained (1st) before exercise and the administration of GLN or water, (2nd) immediately after exercise and (3rd) 30mins, (4th) 1hr, (5th) 3hrs and (6th) 6hrs post exercise. WBC increased ($p<0.05$) immediately after exercise, returned to baseline 30min post exercise but were slightly increased ($p<0.05$) 3 and 6hrs post exercise for the GC. Lymphocyte count in both conditions and % lymphocytes in CC, increased ($p<0.05$) immediately after exercise. Lymphocytes decreased below baseline values from 30min (not significantly for GC) up to 1hr post exercise. The % lymphocytes fell below baseline values ($p<0.05$) from 30min up to 3hrs for CC and 6hrs for GC. Lymphocytes decrease at 1hr post exercise and % lymphocytes decrease 30min and 1hr post exercise were of greater extent ($p<0.05$) in CC compared to GC. Exhaustive resistance exercise seems to result in a transient increase of plasma WBC and

lymphocyte count followed by a short-term decrease in the next few hours. Oral glutamine supplementation reduces lymphocyte decrease after exercise and induces a relatively faster return to baseline. Further research is required, however, to examine whether a causal relation exists.

36 - MOOD STATES AND CYTOKINE CORRELATION IN FEMALE SOCCER PLAYERS WITH AND WITHOUT PREMENSTRUAL SYNDROME (PMS)

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Keywords: inflammation, cytokines, mood states, Premenstrual syndrome, soccer

Introduction: PMS is defined as a group of physical and behavioral changes beginning in the luteal phase and ending during menstruation[1]. It's known that intense physical activity is closely associated with changes in many aspects of immune response, such as cytokine production[2] as well as that cytokines act on behavior and mood states[3-5]. The aim of this study was to evaluate mood states and its relation with cytokine production in female soccer players with (PMS) and without PMS (nPMS) in 4 moments: before and after the game and in the two phases of the menstrual cycle: follicular and luteal. **Methods:** Fifty-two eumenorreic soccer players were evaluated (age:19.8 ± 4.7 years). The PMS and phases of the menstrual cycle were determined by monitoring for 3 consecutive months. Evaluation of cytokines IL-1β, IL-6, IL-8, IL-10 and TNF-α were performed in urine and quantified by Flow cytometry method. The renal function was normal, as could be verified through creatinine analysis. Mood states were evaluated through the Brunel mood scale. This study was approved by the Ethics Committee in Research, from UNIFESP

(No.1604/10). ANOVA and Spearman correlation with significance level of 5% were used for data analysis. **Results**: No difference in renal function was found in both groups and in the 4 evaluated moments. The group nPMS showed a positive correlation of IL-10 with vigor (p=0,05, r = 0,45) and a negative correlation of IL-10 with fatigue (p=0,05, r =-0,45) in luteal phase, pre-game. The PMS group revealed positive correlations of IL-1β in the follicular phase, post-game with anger (p=0,05, r = 0,37) and tension (p=0,01, r = 0,52); as well as the IL-1β with tension (p=0,05, r = 0,36) in the luteal phase, post-game. **Discussion**: The correlation observed in the group nPMS reveals that IL-10 has a positive correlation with vigor. Moreover, the IL-1β may contribute to the worsening of anger and tension behavioral states in the group PMS. In addition, our group has demonstrated that athletes with PMS are affected by an inflammatory state with higher levels of pro-inflammatory cytokines production. **Conclusion:** The results observed in this study show that the anti-inflammatory cytokine is correlated with the emotion considered positive in the nPMS athletes, while the considered negative emotions are shown to be correlated with pro-inflammatory cytokine in the PMS athletes, reinforcing that the expression of different emotions in sport environment can be influenced by neuro-immuno-endocrine mechanism.

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37 - EXPERIMENTAL IMMUNOSTRENGTHENING PRACTICES OF HIGH PERFORMANCE SPORT: HOLISTIC FITNESS APPROACH

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Holistic fitness approaches to high performance training in Australia, China, Eastern Europe and United States have integrated various methods of physical and psychological training, as well as medical, physiotherapy, diet and nutritional methods believed to maximize strength, endurance, flexibility and other performance qualities and prevent illnesses and injuries. Advanced physical training methods included guidelines for lifelong fitness and gradual healthy long term sport-specific athlete development, comprising of cybernetic periodization and parametric training utilizing three sport practices a day in a search for the most efficient and individualized balance of work and rest for the highest desired performance. These methods minimize overtraining and weakening of the immune system. These systems utilize sequences of outdoor dynamic yoga, tai chi and tsigun integrated with weight and water training rationalized for strengthening while stretching and for full body activation (including eye and other small muscles) through compound exercises targeting multiple muscle groups at once. Programming is designed for stimulating the central nervous system—all enriched through natural effects of sun, air and water. Psychological tools for mental strength and efficient rest supporting the immune system include such methods as autogenic training, lucid dreaming, breathing and voice exercises, mindfulness, hypnosis & self-hypnosis as well as color, light and music therapy. Training is also supported by restoration therapies using heat, cold and contrasting temperatures, particularly sauna. Balneotherapy and various hydrotherapies are utilized. Post-training massage and manual therapy include mobilizing traction and analgetic puncture of body points and zones. These and other relaxation and restoration methods are aimed at decompression and prevention of the most important spine disorders suffered by most of people, particularly athletes. Immune responses are also stimulated and balanced through cupping, icing testicles, acupuncture and acupressure as well running and walking on a variety of uneven surfaces, particularly barefoot. Elite athletes now try to eat based on ancient traditions and search for immunostrengthening, neurohacking,

antibacterial, anti-inflammatory and bioactive diets, separating and cross-enhancing different foods. Pre- and probiotics, but also single micronutrients incorporated into functional foods contribute to an enhancement of immunocompetence, stressing the positive role of selenium and dietary antioxidants. High performance sport diets strive for synergy of nutrients and individualization of healing foods experimenting with raw and salted recipes; soups; anti-infection roots, spices and greens; anti/pro inflammatory foods; sizes of portions and fasting, separation and digestion—treating disorders with food and minimizing pharmaceuticals.

38 - TRAINING INFLUENCES THE ACUTE IMMUNE RESPONSE TO A MAXIMAL SWIMMING TEST

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Long-term endurance sports training influence on the acute immune response to exercise has been poorly studied, despite the complexity of both chronic and acute adaptations induced by training programs performed throughout the athlete's career. We aimed to evaluate the effects of training on the systemic and mucosal immune acute response to a maximal swimmingtest at 3 moments of a 4-month training cycle, in swimmers.

Thirteen competitive swimmers (7 females, 6 males, 13 - 20 yrs) performed an incremental maximal step test (7x200 m front crawl) in 3 moments of the season: M1 - after a recovery microcycle, M2 - after a 5 week period of aerobic overload (volume

increased by 20%) and M3 - after 8 weeks of progressive decrease of volume and maintenance of intensity. Fasted blood and saliva samples were collected immediately before (6:30 a.m.) and 5 min after the swimming test, by standard procedures, for the assessment of leukogram (automated counter), lymphocytes subsets including $CD3^+$, $CD4^+$, $CD8^+$, $CD16^+$ and $CD19^+$ (Flow cytometry), serum immunoglobulin A (serum IgA; Nephelometry) and saliva IgA (sIgA; ELISA). sIgA secretory rate (srIgA) was calculated from sIgA values. ANOVA for repeated measures, Friedman, and Wilcoxon tests were used for the assessment of training and sex effects. Statistical significance was set at $p<0.05$.

The magnitude of the increase of leukocytes, total lymphocytes and subsets $CD3^+$ and $CD4^+$ in response to the exercise test was greater at M3 compared to M1 in the whole group, and mean values for males were higher than for females. The magnitude of the leukocytosis and lymphocytosis was also greater at M3 compared to M2. Inversely, the magnitude of the decrease of the $CD4^+/CD8^+$ ratio was smaller at M3. Regarding $CD16^+$, the magnitude of its increase was greater at M3 compared to M1, but only in females. No significant differences were observed between the responses of $CD8^+$, $CD19^+$, IgA, sIgA and srIgA to the exercise tests. Swimmers increased the performance achieved in the maximal test from M1 to M2 and M3.

During this training cycle, it was observed a stimulation of the systemic immune responsiveness and the maintenance of mucosal immune responsiveness to a maximal swimming exercise. Male swimmers had higher responsiveness of leukocytes, total lymphocytes and of the acquired immunity, represented by $CD4^+$ subsets, and contrarily, females had higher responsiveness of innate immunity, represented by $CD16^+$ subsets, at M3.

Although it is difficult to state if these changes reflect positive or negative adaptive mechanisms, training seems to be a main determinant of immune changes in the acute response to maximal exercise.

39 - ANXIETY AND PERCEIVED PSYCHOLOGICAL STRESS PLAY AN IMPORTANT ROLE IN THE IMMUNE RESPONSE AFTER EXERCISE

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Keywords: Running, Immunity, In vivo, Diphencyprone, STAI

There are common pathwaysby whichpsychological stress and exercise stress alter immunity (Perna et al., 1997), and there has been a recent call to physiologists (Wehrwein & Carter, 2016) and exercise immunologists (Walsh & Oliver, 2016) to incorporate objective psychological measurements in their human studies. However, it remains unknown whether psychological stress plays a role in the *in vivo* immune response to exercise. The aim of this study was to examine the relationship between anxiety and perceived psychological stress reported before exercise and *in vivo* immunity after exercise using skin sensitisation with Diphenylcyclopropenone (DPCP).

Sixty-four males completed widely used psychological instruments to assess state-anxiety and perceived psychological stress before exercise, and ran either 30 minutes at 60% (30MI) or 80% (30HI) $\dot{V}O_{2peak}$, 120 minutes at 60% (120MI) $\dot{V}O_{2peak}$ or rested (CON) before DPCP sensitisation. Cutaneous recall to DPCP was measured 4-weeks after sensitisation.

After accounting for exercise (R^2=0.20; P<0.01), multiple-regression showed that pre-exercise state-anxiety (STAI-S; ΔR^2=0.19; P<0.01) and perceived-stress (ΔR^2=0.13; P<0.01) were associated with the DPCP response after exercise. The STAI-S scores before exercise were considered low-to-moderate (median split; mean STAI-S of low, 25 and moderate, 34) and further examination showed that the DPCP response after exercise (30MI, 30HI or 120MI) was 62% lower in low *vs*. moderate state-anxiety (P<0.01).

In conclusion, state-anxiety and perceived psychological stress levels before exercise play an important role in determining the strength of the *in vivo* immune response after exercise. As such, investigators should account for psychological stress when examining the immune response to exercise.

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40 - INFLUENCE OF A-ACTININ-3 (ACTN3) ON INFLAMMATORY MARKERS AFTER ENDURANCE EXERCISE

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The impairment on performance is induced by many factors such as muscle injury follow inflammation. Many researchers have been investigating the role of genetic factors to the phenotypic responses of inflammation. The genotypes of α-actinin-3 (ACTN3) genes have been associated to skeletal muscle resistance and power. ACTN-3 is a major structural component of the Z line in the sarcomere and may modulate of muscle force output at high contraction velocities. The aim of this study was associate the ACTN-3 RX polymorphisms to inflammation induced by endurance exercise. Sixty male endurance runners participated in this study. Blood samples (30 mL) were collected 24 h before, immediately after, 24 h after, 72 h after, 15 days after the São Paulo International Marathon 2015 (60 amateurs runners, 15-17°C and

relative humidity of 82%). The following parameters were carried out to evaluate inflammation: C-reactive protein, alpha glycoprotein, leukocytes count, ACTN-3 RX polymorphism. The demographic data for these subjects are summarized as follows: age, 34 ± 6 years; height, 174 ± 0 cm; body mass, 74 ± 1 kg; % of fat mass, 20 ± 0.5; body mass index, 25 ± 0.2 kg/m^2; average training race 56 ± 2,2 km/week; frequency of training 4,4 time/week; time on 10 km race 46± 0.7 minutes. Marathon race induced an increase onleukocytes (3-fold, $p<0.0001$), neutrophils (4-fold, $p<0.0001$), and monocytes (2-fold $p<0.0001$) returning to basal levels 1 to 3 days after race. CRP elevated 1 day after race (2-fold, $p<0.0001$) and not returned to basal levels after 15 days. Alpha-glycoprotein increase immediately after race and returned to basal levels 15 days after race. We also observed a decrease on eosinophils (5-10-fold) and lymphocytes (by 50% approximately) immediately after race. We not observed difference between RR, RX and XX ACTN-3 genotypes on leukocytes, neutrophils and monocytes count. In RR ACTN-3 genotype, lymphocytes ($p<0.05$) and eosinophils ($p<0.05$) were higher before race and CRP were lower after race ($p<0.05$). Alpha-glycoprotein tended to be lower before and after race in RR ACTN-3 genotype ($p>0.05$). RR ACTN-3 genotypes have lower inflammatory response induced by exercise and high levels of lymphocytes and eosinophils.

41 - CYTOTOXIC ACTIVITY OF NN-32 TOXIN FROM INDIAN SPECTACLED COBRA VENOM ON HUMAN BREAST CANCER CELL LINE

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Animal venoms and toxins are potential bioresources that have been known to mankind as a therapeutic tool for more than a century through folk and traditional medicine. The present study was an effort to establish the anticancer activity of the purified protein toxin (NN-32) from Indian Spectacled Cobra *(Naja naja)* venom in

Human breast cancer cell line. Isolation and purification of NN-32 was done through CM-cellulose ion exchange chromatography and RP- HPLC. Molecular weight was found out by SDS-PAGE. The anti-leukemic activity using MCF-7 cell line was established through cytotoxicity study. NN-32 was eluted with 0.5M NaCl on CM-cellulose ion exchange chromatography. SDS-PAGE molecular weight was found to be 6.7 KDa. NN-32 produced time and dose dependent cell (MCF-7) growth inhibition. It exhibited DNA fragmentation and comet formation in MCF-7 cells. NN-32 produced membrane disruption, blebbing and nuclear disintegration in MCF-7 cells observed through scanning electron microscopy. NN-32 produced apoptosis, cell cycle arrest at G1 phase. NN-32 induced apoptosis in leukemic cells was followed through caspase 3 and 9 pathway activation. It may be concluded that NN-32, a 6.7 KDa protein purified from *Naja naja* venom would be a novel pro-apoptotic agent that induced cancer cell killing through p53 and caspase pathway. It is expected that this study may add new information on anticancer effects of *Naja naja* snake venom, which may be utilized for future drug development clue against cancer.

42 - EFFECT OF MODERATE PHYSICAL EXERCISE ON LEUKOCYTE PROFILE IN TUMOR MICROENVIRONMENT AND MELANOMA GROWTH IN MICE ON A HIGH-FAT DIET

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Keywords: cytokines, M1 macrophages, B16F10 cells, cancer and obesity.

Abstract

Obesity leads to a systemic chronic inflammation promoting an increase in the risk of cancer development. Scientific evidences suggest that moderate physical exercise can be used to modulate the control of inflammation. Therefore, the aim of this study was to evaluate the alterations in leukocytes in tumor microenvironment of animals under high fat diet and moderated physical exercise in a murine melanoma model. Female mice were divided into 8 groups: 1) normal-fat control (N); 2) normal-fat + melanoma (NM); 3) high fat control (H); 4) high fat + melanoma (HM); 5) normal-fat control + moderate exercise (NE); 6) normal-fat melanoma + moderate exercise (NEM); 7) high fat control + moderated exercise (HE); 8) high fat melanoma + moderate exercise (HEM). After eight weeks of diet treatment and application of moderate physical exercise protocol (60 min., 5 days per week), the melanoma was induced by applying B16F10 cells, or phosphate buffered saline (PBS) in the control group. Initially, animals were followed until the death to establish the survival curve. Afterwards, another group of mice were analyzed and euthanized 21 days after injection of tumor cells. Food consumption, body weight, growth, physical performance, gastrocnemius and soleus muscle citrate synthase activity, tumor growth, tumor weight and adipose tissues weight were determined. Histological analysis of the tumor microenvironment was also performed. T regulatory (Treg) cells ($CD4^+/CD25^+/FoxP3^+$) and Th17 cells ($CD4^+/IL\text{-}17A^+$), M1 and M2 macrophages infiltrated into the tumor was determined by flow cytometry. Cytokine profile (IL10, IL12, MCP-1, IFN-gamma, TNF-alpha and IL6) in tumor tissue was assessed by CBA assay. We observed that animals subjected to high fat diet had higher energy consumption (30% on average) and body weight gain (H and HE vs N and NE 37%, HM and HEM vs NM and NEM 73%, respectively). Animals subjected to exercise training showed higher physical performance (N and NM vs NE and NEM 35%; H and HM vs HE HEM and 26%, respectively). Animals from HM group presented higher tumor growth in comparison to all groups. Physical exercise promoted a lower tumor development. In tumor microenvironment, we observed higher M1 macrophage infiltration in animals from HM group. Exercised mice presented lower M1 macrophage percentage and an increase of M2 macrophages. These data indicate that moderate physical exercise can attenuate the inflammatory response from macrophages induced by high fat diet leading to a decrease of tumor growth.

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43 - EFFECTS OF EXERCISE TRAINING ON PROSTATE DIMENSIONS IN A RAT MODEL OF PROSTATE CANCER

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Keywords: prostate cancer, prostate dimensions, rat, ultrasonography

Cancer is one of the most frightening diseases worldwide. Prostate cancer is one of the most frequent cancers among men (WHO, 2015). The present work aimed to evaluate the effects of exercise training on prostate dimensions in a rat model of prostate cancer.

All experiments were approved by the Portuguese Ethics Committee. Ninety-five male Wistar rats of four weeks of age were divided into four experimental groups: flutamide sedentary (n=25), flutamide exercised (n=30), control sedentary (n=20) and control exercised (n=20). At eight weeks of age, animals from exercised groups started an exercise program on a treadmill (Treadmill Control® LE 8710, Panlab, Harvard Apparatus, Holliston, MA, USA): 5 days/week, gradually increased from 20 min/day to 60 min/day and speed also increased from 15 m/min to 30 m/min. Four

weeks later, the multistep protocol of the induction of prostate cancer was started through the subcutaneous administration of the antiandrogenic drug flutamide to animals from flutamide groups (50 mg/kg of body weight) for 21 consecutive days. Forty-eight hours later, animals received an intraperitoneal injection of the carcinogen agent *N*-methyl-*N*-nitrosourea (MNU) (30 mg/kg of body weight). The prostate dimension were non-invasively evaluated by ultrasonography (Logiq P6®, General Electric Healthcare, USA) before the beginning and immediately after the end of the flutamide administration, and six weeks after the end of flutamide administration. The exam was recorded and the images with bigger dimensions (images with the highest area, Area=π×r1×r2, where r1 is the bigger radius and r2 the small radius) were selected. The radius of the ventrolateral lobes of the prostate were measured using the integral calipers of the ultrasound apparatus (the cursors were set at the borders of the prostate). The prostatic area of each animal resulted from the sum of the left and right ventrolateral lobes area.

The prostate dimensions before the flutamide administration (first ultrasonographic examination) were similar among groups (p>0.05). A decrease in prostate dimensions was observed between the first and the second ultrasonographic examination in flutamide-exposed groups; conversely an increase was observed in control groups (p<0.05 from="" flutamide="" groups="" prostate="" dimensions="" increased="" in="" all="" between="" the="" second="" and="" last="" ultrasonographic="" examination="" being="" this="" increase="" more="" pronounced="" flutamide-exposed="" em="">p<0.05). No differences were observed between exercised and sedentary groups. The exercise training did not change the prostate response to the antiandrogenic drug flutamide and the carcinogen MNU.

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44 - RESISTANCE TRAINING REDUCES T HELPER CYTOKINE LEVELS BUT NOT CARDIOMETABOLIC RISK FACTORS IN HIV-INFECTED INDIVIDUALS RECEIVING ART

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Lipodystrophy syndrome and cardiometabolic diseases are conditions that affect HIV-infected individuals on ART. A shift from T helper (Th) 1 to Th2 cytokine profile is associated with disease progression in these individuals and has been linked with lipodystrophy. Resistance training (RT) in combination with protein-containing nutrition has been considered an important tool to improve strength and body composition. The aim of this study was to determine the effect of combined RT and whey protein on body composition, Th1 and Th2 cytokines and cardiometabolic risk in HIV-infected individuals receiving ART. Methods: Forty HIV-infected participants (40.8 ±7.7 yrs, 70.8 ±16 kg, BMI 30.9 ±7.2 kg/m2) receiving ART (≥18 months) were randomly assigned either whey protein/progressive resistance training (PRT) (n=18), placebo/PRT (n=14) or as a control (n=8). Participants received either 20g whey or placebo (maltodextrin) pre and immediately post each PRT session. Whole body RT was performed 2/week for 3 months with loads progressing from 40-85% of one repetition maximum (1RM). Measurements including height, weight, waist, hip, DEXA and 1RM testing were performed 48-72 hrs before (pre = T1) and after 3 months (T2) PRT program and 3 months (T3) following cessation of the PRT program. Additionally, venepuncture was performed to measure systemic immune,

inflammatory and cardiometabolic risk markers. Statistical analysis included two-way ANOVA with multiple comparisons in the PRT groups and one-way ANOVA with repeated measures in the control group. Alpha was set at $p \leq 0.05$. Results: There was a significant ($p < 0.001$) main effect of time for PRT groups and control group for the HOMA-IR index. Post-hoc testing demonstrated that HOMA-IR index significantly increased from T1 to T2 ($p = 0.002$) and from T1 to T3 ($p < 0.001$) for placebo/PRT and whey/PRT groups, respectively. There was significant ($p = 0.05$) main effect of time for PRT groups for the Th2 cytokine IL-10. There was a significant main group effect for the immunity marker CD8% ($p = 0.05$), anti-inflammatory markers IL-10 ($p = 0.01$), IL-13 ($p = 0.05$) and the pro-inflammatory marker IL- 12 ($p = 0.02$). Post hoc testing revealed a significant group effect with placebo/PRT lower over the 3 time points for IL-10 ($p = 0.008$) and IL-12 ($p = 0.016$). Conclusion: HIV serves as both a metabolic and an inflammatory challenge. Our study demonstrated that a PRT programme can decrease anti-inflammatory and pro-inflammatory cytokines possibly reflecting reduced systemic inflammation in HIV-infected individuals.

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45 - ADIPOKINES LEVELS IN RESPONSE TODIFFERENT INTENSITY PHYSICAL EXERCISE PROTOCOLS IN YOUNG HEALTHY MEN

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Keywords: Adipokines, Aerobic Exercise, Intensity.

Introduction and objective: Adipose tissue is considered an endocrine organ that secretes bioactive peptides involved in autocrine, paracrineand endocrine functions, named as “adipokines”[1].There are three classical adipokines,adiponectin, leptin and resistin, which, respectively, exert anti-inflammatory actions, food intake control and pro-inflammatory effects[2]. Currently, the modulatory effects of physical exercise on adipokine levels have been recognized,[2] although there is scarce data comparing protocols of physical exercise with different intensity. Therefore, we assessed the acute effect of high and moderate intensity protocols of physical exercise on plasma and urine levels of adipokines. **Subjects and methods:** Thirteen young healthy physically active men were recruited to four supervised training sessions. Two evaluation sessions were performed to measure body composition, physical activity, aerobic and anaerobic capacities before High-Intensity Interval Exercise (HIIE) and Moderate-Intensity Continuous Exercise (MICE) iso-work exercise sessions on a cycle ergometer. The HIIE protocol included a 5-minute warm-up at 60-70% of heart rate peak (HRp) intensity followed by 10 sets of 30 seconds above 90% with 1 minute of recovery and 3 minutes of cool down (both at the same warm-up power). MICE protocol was performed at constant power corresponding at 60-70% of HRp and finalized at the same total work of HIIE. Blood and urine samples were collected before and after the exercise protocols, then stored at -80°C for furtheranalysis of adipokine content (adiponectin, leptin and resistin) by enzyme-linked immunoassay (ELISA). **Results:** Plasma and levels of leptin,resistin and adiponectin did not differ in the comparison between baseline concentrations (before exercise protocols) and between levels after both exercise protocols. Urine concentrations of resistin and leptin also did not differ at baseline and after both exercise protocols. However, urine levels of adiponectin significantly increased after HIIE protocol (p=0,0005). In addition,the concentrations of adiponectin in urine were significantly higher following HIIE than after MICE (p=0.0039). **Conclusion:** Our study showed that the HIIE protocol induced a more intense increase in urine levels of adiponectin concentration in comparison to MICE. This result suggests that HIIE may be an interesting training intervention in order to improve metabolic profile.

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46 - EXHAUSTING EXERCISE IN YOUNG RATS: EFFECT ON SYSTEMIC AND INTESTINAL LYMPHOID TISSUES

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Keywords: exhausting exercise, mucosal immune system, lymphoid tissues

While moderate exercise has an enhancing effect on immune system, exhausting exercise can be harmful (Gleeson, 2007; Kruijsen-Jaarsma *et al.*, 2013). In this context, animal models in which an exercise-derived immunodepression could be reproduced are very limited. The aim of this study was to establish immune markers of exhausting exercise both in the systemic and mucosal lymphoid tissues of rats reflecting the depression of the immune function.

Young female and male Wistar rats were trained in an increasing procedure in a treadmill for 4 weeks. Afterwards, rats were submitted to an exhaustion protocol in the same treadmill. Blood and faeces were collected throughout the study. Macrophages were isolated from peritoneal cavity and small intestine were dissected. In addition, the weight of gastrocnemius muscle, heart and lymphoid tissues were registered.

Results showed a different exercise pattern between males and females, being young females better runners than young males. Runners had higher gastrocnemius muscle and heart weights than sedentary rats, whereas spleen and thymus weight

were lower in runner rats. Reactive oxygen species increased in macrophages from runner rats. Intestinal immune markers showed that faecal IgA decreased by training. In addition, the gene expression of occludin (as a marker of intestinal barrier function) was reduced in runner rats whereas that of mucin was increased.

In conclusion, the increasing training exercise applied in rats for 4 weeks followed by an exhausting session produced a harmful effect on systemic and intestinal immune system that can be quantified by lymphoid tissue weights and faecal IgA, as well as intestinal barrier markers.

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47 - PHYSICAL EXERCISE WITH DIFFERENT INTENSITIES ACUTELY MODULATES BOTH AXES OF THE RENIN-ANGIOTENSIN SYSTEM IN HEALTHY SUBJECTS

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Keywords: Renin-angiotensin system, Exercise, Intensity

Introduction: The renin-angiotensin system(RAS) has two opposite arms, the classical one, formed by angiotensin converting enzyme(ACE), Angiotensin II(Ang II) and AT1 receptor that exerts vasoconstriction and pro-inflammatory actions, and the

counter-regulatory, composed by ACE2, Angiotensin-(1-7) [Ang-(1-7)] and Mas receptor, which elicits vasodilation and anti-inflammatory effects[1]. In this regard, experimental studies have suggested that changes in both RAS axes may contribute to the beneficial role of physical exercise in chronic diseases related to inflammation[1]. However, there is no data comparing the effects of different intensity protocols of exercise on both RAS axes in healthy individuals. Therefore, we investigated the acute effect of two protocols of physical exercise in urine and plasma levels of RAS components. **Subjects and methods:** Thirteen young healthy physically active men were recruited to four supervised training sessions. Two evaluation sessions were performed to measure body composition, physical activity, aerobic and anaerobic capacities before High Intensity Interval Exercise(HIIE) and Moderated Intensity Continuous Exercise(MICE) iso-work exercise sessions on a cycle ergometer. The HIIE protocol included a 5-minute warm-up at 60-70% of heart rate peak(HRp) intensity followed by 10 sets of 30 seconds above 90% with 1 minute of recovery and 3 minutes of cool down (both at the same warm-up power). MICE protocol was performed at a constant power corresponding to 60-70% of HRp and finalized at the same total work of HIIE. Blood and urine samples were collected before and after the protocols, then stored at -80°C for further analysis by enzyme-linked immunoassay(ELISA). Plasma and urine levels of ACE, ACE2, Ang-(1) and AngII were measured before(baseline values) and after both exercise protocols. **Results:** HIIE protocol had a significant increase of ACEurine levels and ACE2plasma levels($p=0.0098$ and $p=0.0161$, respectively).Urine concentrations of ACE2 and of Ang-(1-7) significantly raised after MICE protocol($p=0.0184$ and $p<0.0001$, respectively).When comparing these variations in RAS components between both exercise protocols, a more intense reduction of plasma and of urine levels of ACE($p=0.0144$and$p=0.0042$, respectively) in line with a greater increase ofurine concentrations of Ang-(1-7)($p=0,0059$)occurred in MICE protocol. **Conclusions:** Moderate intensity exercise showed more intense stimulation of the counter-regulatory RAS axis and HIIE protocol exerted more intense effects on the classical RAS axis. Further studies are needed to elucidate the precise meaning of these acute changes in both RAS axes following exercise.

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48 - FATIGUING EXERCISE ALTERS LEUKOCYTE SUBPOPULATION FREQUENCY IN THE BONE MARROW AND PERIPHERAL BLOOD IN C57BL/6 MICE

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Keywords: physical exercise, immune function, leukocytes.

Previous studies have demonstrated the influence of intense exercise on immune function including changes in the population of leukocytes such as neutrophils, lymphocytes and monocytes on the blood circulation. A common finding is that the numbers of leukocytes subpopulation alters after different protocols of exercise. **Aim:**Here, we investigated the effects of progressive fatiguing exercise protocol on the leukocytes frequency on the blood circulation and in the bone marrow in the C57BL/6. **Methods**: An electric treadmill was used for the fatiguing exercise protocol. The initial speed was set at 5 meters per minute (m/min) for 30 minutes to familiarize the mice with the apparatus and task. The speed was then increased 1 m/min every 3 min, at a 5% grade, until the animal stopped running and was fatigued, which was judged by the refusal of the mouse to continue moving on the treadmill belt more than 10 seconds. The control group did not perform fatiguing exercise protocol and exercised group exercised until fatigue by running for 56.3 ± 6.8min. Blood and bone marrow were collected by 1 h after the end of exercise and analyzed in flow cytometry for the following markers: Ly6C-monocytes, Ly6G-neutrophils and CD3-T cells. **Results:** The results show that after 1 hour of the end of fatiguing exercise

protocol, C57BL/6 mice, there was an increase in the frequency of neutrophils (from 22.8% to 48.6%) and monocytes (from 34.8% to 70.5%) in the blood while there was elevation of the lymphocyte population (from 5.5% to 8.1%) in the bone marrow. We believe that this profile may undergo modifications in later times and we are working in this proposal. **Conclusion:** Taken together, these results suggested that the fatiguing exercise protocols induces immunological changes and provokes significant, although transient, modulation of the immune system, specifically of the leukocyte sub-population.

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49 - EFFECTS OF ACUTE EXHAUSTIVE EXERCISE ON MONOCYTE SUBSETS AND EPIGENETIC MARKERS IN PERIPHERAL MONONUCLEAR CELLS OF LEAN AND OBESE MALES

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Keywords: obesity, Histone H4, HDAC activity, monocytes, exhaustive exercise.

Introduction Excess of fat mass are associated with chronic low-grade inflammation, elevation of 2-3 folds on inflammatory mediators[1]. Despite evidences showing the pro inflammatory peripheral mononuclear cells (PBMC) state in obesity[2], little is known about the epigenetic modulation under basal or exercise conditions. **Methods** This study was approved by Ethics Committee of UFCSPA.Eight lean (BMI <24.9 kg="" m="" and="" eight="" obese="" bmi="">30.0 to 35.0 kg/m²) sedentary

men were submitted to a single bout of exhaustive stepping exercise, consisting of 1 s up and down cycles to fatigue with a 30 s recovery period. Following each 30 s recovery participants recommenced the stepping cadence until fatigue prevented them continuing. Blood samples was collected pre and immediately post-exercise. Monocyte phenotype was determined in accordance to the expression of CD14 and CD16 by flow cytometry. PBMC (1.5 x 10^6 cells/mL) were isolated and stimulated *in vitro* with lipopolysaccharide (LPS, 10 ng/mL) or media. After 24h, cells were collected for analysis of global histone H4 acetylation levels (H4ac) and HDAC2 activity, and the supernatants were used for IL-6, IL-8 and TNF-a quantification. **Results** At rest, obese individuals presented higher frequency of $CD14^+CD16^+$ pro inflammatory monocytes than lean individuals ($p<0.05$). Moreover, non-stimulated PBMC from obese presented low HDAC2 activity ($p=0.03$) and higher TNF-a ($p=0.01$) and IL-8 ($p=0.02$) production than lean. LPS-stimulated PBMC of obese group had higher H4ac ($p=0.01$), low HDAC2 activity ($p<0.01$) and a pro inflammatory profile characterized by increased levels of TNF-a, IL-6 and IL-8 than lean group ($p<0.01$ for all). A single bout of exhaustive exercise had an overall pro inflammatory effect in both groups of lean and obese, evidenced by: 1) increased IL-8 and TNF-a production by LPS-stimulated PBMC immediately after exercise compared to baseline ($p<0.02$ for all); 2) increased peripheral frequency of $CD14^+CD16^+$ cells after exercise ($p<0.04$). Regarding epigenetic markers, both non-stimulated and stimulated PBMC from obese individuals presented a global H4 hyperacetylation status ($p=0.01$ under non-stimulated; $p=0.04$ stimulated condition) after exercise. A significantly reduction in HDAC2 activity in PBMC was observed after exercise in non-stimulated ($p=0.022$) and stimulated ($p=0.030$) conditions in obese group.

Conclusion The data indicates that epigenetic events occur in conjunct to pro inflammatory monocyte polarization and augment of inflammatory cytokines at rest and after a single bout of exhaustive exercise. In addition, obese individuals present a hyperacetilation histone H4 status that could influence the subclinical inflammatory status of PBMC.

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50 - CARDIORESPIRATORY FITNESS MODULATES THE ACUTE RESPONSE OF MEMORY TREG AND MEMORY EFFECTOR OF T CELLS TO INTERVAL EXERCISE IN OBESE MEN

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Keywords: Treg, interval exercise, obesity, CD39.

Introduction The ectonucleotidase CD39 is an enzyme that are highly expressed in regulatory T cells (Treg) and involved in adenosine production that contributes to Treg immunosuppression activity[1]. It was recently identified that $CD4^+CD25^+CD39^+$ T cells denotes a memory Treg (mTreg), while $CD4^+CD25^-CD39^+$ T cells exhibit the memory effector cellular phenotype (mTeff)[1]. Although it is widely accepted that cardiorespiratory fitness can modulate the frequency of Tregs[2] and memory phenotype T cells[3], little is known about the influence of acute exercise on $CD4^+CD25^{+/-}CD39^+$ T cell populations in obese individuals with different degrees of cardiorespiratory fitness. The aim of the present study was to evaluate the acute response of distinct $CD4^+CD25^{+/-}CD39^+$ T cell populations to interval exercise in obese men. **Methods** This study was approved by Ethics Committee of UFCSPA.Sixteen abdominally-obese men (BMI>28.5 kg/m², AC>90 cm) were stratified into lower- (VO_{2Peak}=33.4±5.05 mL.kg.min, n=8) and higher-fit (VO_{2Peak}=47.1±5.1 mL.kg.min, n=8) groups. The participants underwent an interval exercise session on a motorized treadmill, consisting of five bouts of 3 minutes (85% of Maximal Heart Rate) with 3 minutes of active recovery (50% of Maximal Heart Rate). Blood lymphocytes were collected before, immediately after, and 60 minutes after interval exercise to analyze the expression of CD25 and CD39 into $CD4^+$T cells. The interleukin-17a (IL-17a) and interferon-gamma (IFN-g) was evaluated in samples

of serum and supernatants of PBMC after stimulation with phytohemagglutinin (PHA) *in vitro*.

Results At baseline, lower-fit group presented diminished frequency of mTreg than higher-fit groups (p=0.005). After a single bout of interval exercise, circulating mTreg cells increased immediately after (p=0.02), and remained higher 60 minutes after bout (p=0.03) in higher-fit individuals. On the other hand, lower-fit participants demonstrated only an elevation in mTreg cells after 60 minutes of interval exercise (p=0.04). Although, $CD39^{+}$mTeff cells tended to be lower immediately after exercise in higher-fit group (p=0.06), no significantly changes was observed in $CD39^{+}$mTeff cells after interval exercise in both groups (p>0.05). In addition, no significantly changes were observed in IL-17a and IFN-g production after exercise in both groups (p>0.05) or conditions (serum and PHA-stimulated PBMC).

Conclusion Cardiorespiratory fitness influences the frequency of mTreg and mTeff cells of peripheral blood of obese individuals in response to a single bout of interval exercise. The enhanced mTreg frequency observed after exercise could explain the absence of pro inflammatory cytokines elevation post interval exercise.

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51 - EXERCISE IS MORE EFFECTIVE THAN METFORMIN TO IMPROVE HEALTH RELATED QUALITY OF LIFE AND MOOD STATES IN OLDER ADULTS WITH TYPE 2 DIABETES

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Keywords: diabetes, exercise, metformin, mood states, quality of life, older adults.

Introduction Type 2 diabetes (T2D) is a high-impact complex multi-factorial disease that imposes a life-long physical and psychological burden (Aschner et al. 2014), particularly in older adults (Gadsby 2014) due to the added effect of co-morbidities, pharmacological treatment, heterogeneous functional status, low exercise training and frequently disruptive negative effects such as restlessness, distress, anxiety, depression and dementia (Gadsby 2014; Abdelhafiz & Sinclair 2015) reducing the efficacy of T2D management and quality of life (QoL) (American Diabetes Association 2016). Furthermore, while the prevalence of mental health problems in older adults with T2D exceeds values found in the general population (American Diabetes Association 2016), previously inconsistent results, highlight the need to promote the appropriate strategies to improve the mental component of QoL.Therefore, the aim of this study is to analyze the effect of three types of treatment: i) exercise training with multicomponent exercise (E); ii) pharmacologic treatment with oral hypoglycemic drug – metformin (M); and iii) a combined therapy – exercise and metformin (MEX) on health related quality of life (HRQoL) and mood states in older adults with type 2 diabetes (T2D) with comorbidity in an early stage of **Methods:** This un-randomized longitudinal cohort study included 284 T2D older adults (> 60 years) that underwent one of 3 conditions: i) E (n = 59) trained three times/week; ii) M (n = 30) used 850 mg of metformin twice daily; and iii) MEX (n = 195) combined exercise and metformin. Participants completed baseline, and 2-year follow-up evaluations including the Short Form Health Survey 36, Profile of Mood States – Short Form, the health history questionnaires, anthropometric and blood biochemistry. **Results:** After the 24-months intervention, E and MEX revealed improved mood states, with large effect size on the vigor domain, and moderate effect size in the anger, and total mood disturbance domains, in comparison with the M group. The E and MEX groups perceived better physical and mental HRQoL than the M group. Contrarily, the M group unchanged HRQoL domains (P> 0.05). **Conclusions:** Metformin had no significant effect on self-referred HRQoL in T2D participants aged above 60 years, in an early stage of the disease. The E and MEX therapies were the most effective to improve mood states, and HRQoL in older adults with T2D.

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52 - THE EFFECT OF ANTIHYPERTENSIVE MEDICATION AND EXERCISE TRAINING ON FUNCTIONAL STATUS IN HYPERTENSIVE OLDER ADULTS

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Keywords: Diuretics; Calcium channel blockers; β- blockers; Exercise; Functional Status.

Introduction Over the last decade, an increasingly prevalence of functionally-limited hypertensive individuals (Hajjar et al. 2016), highlights the need to identify interventions capable to reduce hypertension- aging- disability burden and maximize an healthy aging (Buford 2016).Thus, in context of the preceding trends, the aims of the present study is to compare the effect of three types of antihypertensive treatment in response to chronic exercise training on functional status in independently hypertensive older adults with comorbidities: *i)* thiazide diuretic's medication (D); *ii)* calcium channel blockers (CCB); *iii)* β- blockers medication (βB). **Methods** This 2-year un-randomized longitudinal cohort study included 96 hypertensive older adults that underwent one of the following 3 conditions: i) thiazide-related diuretics medication (D; *n*=33); ii) calcium channel blockers medication (CCB; *n* = 23); iii) and β-blockers medication (βB; *n* = 40). Baseline and follow-up evaluations included the Senior Fitness Test battery, Short Form Health Survey 36 (SF-36), the health history questionnaires, anthropometric and hemodynamic

profile. **Results** All groups improved the physical functional status, particularly upper and lower body strength and aerobic endurance and systolic blood pressure. The D and βB groups also improved the waist circumference and body mass. The CCB decreased total cholesterol (P = 0,028), presented better physical functioning, physical component score but also augmented bodily pain. The βB group decreased triglycerides (P = 0.013). No group differences were found.

Conclusions Functional status improves with antihypertensive medication jointly with exercise training. Independently of the antihypertensive medication choice, exercise training plus antihypertensive therapy should be recommended into the standard prescription practice to reduce the rate of physical disability among hypertensive older adults.

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53 - INCREASED SKELETAL MUSCLE IL-15Rα IS ASSOCIATED WITH MYOFIBRILLAR PROTEIN SYNTHESIS IN RESPONSE TO A SINGLE SESSION OF RESISTANCE EXERCISE

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Keywords: Myokines, IL-15/IL-15Rα axis, strength training, muscle protein synthesis/breakdown

Introduction: *In vitro* and *in vivo* studies described interleukin-15 (IL-15) and its cognate receptor alpha (IL-15Rα) as agents implicated in the regulation of the anabolic/catabolic balance in skeletal muscle (Quinn et al., 2002; O'Connell et al., 2015). IL-15Rα may have a role in determining the phenotype and fatigability of muscle fibers *per se* (O'Connell et al., 2015; Loro et al., 2015). Despite the potential role of IL-15 and IL-15Rα as anabolic/anti-atrophy agents, direct evidence is lacking and no human study has assessed IL-15Rα expression in skeletal muscle. The aim of the study was to determine skeletal muscle IL-15 and IL-15Rα responses to a resistance exercise session and to analyse their association with myofibrillar protein synthesis (MPS). **Methods:** Fourteen participants performed a bilateral leg resistance exercise composed of 4 sets of leg press and 4 sets of knee extension at 75%1RM to task failure. Muscle biopsies of vastus lateralis were obtained at rest, 0, 4, 24 and 28h post-exercise during a primed-continuous infusion of L-[ring-13C6] phenylalanine to determine rates of MPS and skeletal muscle IL-15 and IL-15Rα expressions by qRT-PCR and Western blot. Blood samples were drawn at rest, mid-exercise, 0, 0.3, 1, 2, 4 and 24h post-exercise. **Results:** Skeletal muscle IL-15Rα mRNA and protein expression were increased at 4h post-exercise by ~2-fold ($P<0.001$) and ~1.3-fold above rest ($P=0.020$), respectively. IL-15 and IL-15Rα mRNAs increased by ~2-fold ($P=0.003$ and $P=0.002$, respectively) at 24h post-exercise. Myofibrillar fractional synthetic rate increase between 0-4h was associated with IL-15Rα mRNA at rest ($r=0.662$, $P=0.019$), 4h ($r=0.612$, $P=0.029$) and 24h post-exercise ($r=0.627$, $P=0.029$). Up-regulation of IL-15Rα protein expression was related to leg press 1RM ($r=0.688$, $P=0.003$) and total weight lifted ($r=0.628$, $P=0.009$). **Conclusions:** IL-15Rα has been previously suggested to play a role in muscle phenotypic adaptation to resistance training (O'Connell et al., 2015; Riechman et al., 2004). The present study confirms that a single session of resistance exercise elicits the IL-15/IL-15Rα signaling pathway activation. The IL-15Rα independent association with MPS indicates that the IL-15/IL-15Rα axis may have a relevant role in human

skeletal muscle remodeling. Further attention is required to understand skeletal muscle IL-15 production from a metabolic and immune perspective.

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54 - WHAT IS THE EFFECT OF A FAST FOOD VERSUS A MEDITERRANEAN MEAL IN THE ADIPOKINE RESPONSE TO AN EXERCISE CHALLENGE?

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Background: Adipose tissue-derived adipokines are pro-inflammatory cytokines thought be involved in metabolic-related diseases. Obesity and poor diet can affect levels of adipokines. Acute exercise challenge can also influence the adipokine, myokine and adipo-myokine response. We aimed to compare the effect of a Mediterranean (MdM) vs. fast food meal (FFM) on the response of adipokines to an

acute exercise challenge. **Methods:** In a double blinded cross over trial, 46 participants were randomly assigned to eating one of two standardized iso-energetic meals: a FFM including a burger, French fries and Cola or a MdM, comprised of vegetable soup, pasta, tomato, olive oil, herbs, garlic, bread, sardines, fruit and water. Three hours after eating the meal, participants completed a treadmill exercise test (EC). After a seven day wash out period, the intervention was repeated with the opposite meal. Blood samples were obtained before and after each meal, and immediately after the EC. Demographic, anthropometric characteristics, moderate-to-vigorous physical activity, dietary intake during wash out period and serum cortisol were assessed and included as potential confounders. Blood level of adipokines were determined by a Luminex magnetic bead immunoassay, with a human adipokine panel (HADK1MAG-61K, EMD Miillipore®) that included Adiponectin, Resistin, PAI-1, Lipocalin-2/NGAL and Adipsin. Wilcoxon signed rank test applied to compare changes before/after meal and before/after EC. A linear mixed model (LMM) was used to evaluate the effect of meals on the adipokine response to exercise. **Results:** Thirty-nine participants (mean age 25 years) completed the trial (56% females). There were no differences in oxygen consumption, carbon dioxide production or respiratory exchange ratio during EC. The post EC heart rate was higher in the group who ate the FFM (p=0.001). In both intervention arms there was a statistically significant reduction of adipsin after each meal (Variation MdM -234.3[-1099.8;197.7]; Variatin FFM -304.5[-623.7;-100.42], with no difference between groups p=0.936). After the EC, adipsin, lipocalin, PAI-1 and resistin, significantly increased in both intervention groups. Results did not differ between meals. Using a LMM, adjusted for confounders, when EC was preceded by a MdM there was a higher increase in adipsin serum levels. PAI-1 and resistin results were similar after adjusting for potential confounders. **Conclusion:** A pre-exercise Mediterranean meal potentiates the increase of adipsin after treadmill exercise test, which possibly relates to the immune regulatory role of adipsin; nevertheless, an increase in adipsin levels has recently been correlated with an improvement of â cell function. Adipsin, PAI-1 and resistin increased after an exercise challenge. This response might vary accordingly to the type and intensity of exercise, therefore should be considered when assessing the adipokine responses to acute or long term exercise interventions.

55 - INFLAMMATORY BIOMARKERS AND OXIDATIVE STRESS ENZYMES IN YOUNG WOMEN UNDERGOING MUSCULAR HYPERTROPHY TRAINING

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Keywords: Chemokines, hypertrophy, oxidative stress enzymes and strength training

The strength training is a fundamental part of a general training performance (sport, health and etc) as well as the muscular hypertrophy is one of its main adaptation. The aim of this study was to identify the levels of chemokines and the oxidative stress enzymes in plasma of young women undergoing muscular hypertrophy training. The untrained women volunteers (n=11) were submitted to training in a knee extensor bench for 3 times/week (in a total of 10 weeks) with a progressive series starting with 3 and ending with 5 series, of the 6 repetitions, at 60% of 1RM (maximum repetition). Each movement was executed in 6 seconds (3s of concentric and 3s of eccentric muscular actions) and recovery of 180s. The quadriceps hypertrophy was estimated by computerized magnetic resonance imaging and the maximal strength by 1RM test, before and after training. The circulating oxidative enzymes (CAT, SOD, Frap and TBARS) were evaluated by colorimetric method while the inflammatory chemokines (IL-8, CCL2 and CCL5) by enzyme immunoassay. All biomarkers were evaluated before and 30 minutes after the exercise at the 1st, 15th and 29th training sessions. Our data shown the muscle hypertrophy and the maximal strength at the end the training period. We observed high levels of CCL2 and FRAP on the first training session and high levels of CCL5 and CAT on the last training session. We also observed an increase of TBARS level in association with the acute exercise response. In summary, the strength training performed in young untrained women, following this described protocol, resulted in hypertrophy and increases in

maximal strength in quadriceps, increase on the CCL5 and CAT with training and decrease on the CCL2 and FRAP to 15th training´s session.

56 - NO EFFECT OF ACUTE OR CHRONIC BOVINE COLOSTRUM SUPPLEMENTATION ON CIRCULATING INSULIN-LIKE GROWTH FACTOR-I

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Keywords:

Introduction The World Anti-Doping Agency does not recommend the consumption of bovine colostrum (COL) as it contains prohibited substances (e.g. insulin-like growth factor-I, IGF-I) that may influence the outcome of anti-doping tests. Our aim was to perform post-hoc analysis of samples collected in three prospective, placebo-controlled randomised trials of COL supplementation and immune health from our laboratory. **Methods** IGF-I concentration was quantified in duplicate pre-treated (to release IGF-I from binding proteins) plasma samples via an enzyme-linked immunosorbent assay. Eighty nine healthy, recreationally active males were included from published (Study 1: Jones et al., 2014, Study 2: Jones et al., 2015) and yet to be published investigations of COL supplementation. We also determined IGF-I concentrations in COL and placebo (PLA) (isoenergetic/isomacronutrient mixture of skimmed milk powder and milk protein concentrate) supplements and commercially available milk products. **Results** COL supplement (70 ng/ml) contained an approximate eight-fold greater level of IGF-I than PLA (8 ng/ml), whole milk (9 ng/ml), semi-skimmed milk (9 ng/ml) and skimmed milk (9 ng/ml). In study 1, compared to placebo (n = 28, baseline: 107 ± 38 ng/ml, 12 weeks: 104 ± 37 ng/ml), 12 weeks of COL (20 g per day) supplementation (n = 25, baseline: 96 ± 26 ng/ml, 12 weeks: 93 ±

24 ng/ml) did not lead to changes in circulating IGF-I (two-factor mixed ANOVA, group: p = 0.400, group x time interaction: p = 0.498, time p = 0.602). In study 2, there were no differences in circulating IGF-I between PLA (n = 10, baseline: 109 ± 27 ng/ml, 4 weeks: 119 ± 35 ng/ml) and COL (n = 10, baseline: 107 ± 21 ng/ml, 4 weeks: 106 ± 21 ng/ml) groups following 4 weeks of (20 g per day) supplementation (two-way mixed ANOVA, group: p = 0.584, group x time interaction: p = 0.083, time p = 0.243). In study 3, two-factor repeated measures ANOVA (group: p = 0.133, group x time interaction: p = 0.166, time p = 0.013) revealed a change over time but not any significant differences in IGF-1 between a total acute dose of 40 g of COL (n = 16, baseline: 130 ± 36 ng/ml, 1 hour: 132 ± 34 ng/ml, 5 hours: 126 ± 32 ng/ml) or PLA (n = 16, baseline: 133 ± 39 ng/ml, 1 hour: 141 ± 39 ng/ml, 5 hours: 133 ± 39 ng/ml). **Conclusion** Despite greater concentration of IGF-I in COL products compared to energy matched PLA supplements and commercially available milk products, these findings provide further evidence that acute and chronic COL consumption do not change circulating levels of IGF-1.

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57 - THE INFLUENCE OF USING DIFFERENT SOUNDS CHICKEN ON IMMUNOLOGICAL AND PHYSIOLOGICAL TRAITS OF BROILER

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This study was conducted at the experimental field of the Department of Animal Resources, College of Agriculture, Sulaymaniyah University, Iraq. from August 24th 2015 to October 4th 2015, the chicks brought from hatchery Kasha in the area Taslojh. it was complementary to first experiment, the sounds treatment that gave the best behavioral and physiological results in first experiment were chosen in this experiment as follow: Movement of Chicken Feet (1), Regular Soft Timid Hens (2), Chicks Care (3) and Control (T4 without sound). Hatched, straight run chicks (n = 160), were randomly distributed among 4 treatments, which with four replicates (2 replicates male and 2 replicates female) per treatment and 40 chicks per replicate (10 chicks/treatment), The results show**:** Significant improvement (P<0.05) of PCV, the total number of WBC, RBC ,hemoglobin concentration, Heteophil %, glucose and total protein Significantly decreased (P<0.05) in H/L ratioconcentration ofuric acid and cholesterol of Movement of Chicken Feet (1) and Chicks Care (3) in 14 and 42 days. Significant improvement (P<0.05) in the concentration of the hormone prolactin to Movement of Chicken Feet (1), Regular Soft Timid Hens (2), Chicks Care (3). in the period before exposure to sound 30 minutes before exposure directly after exposure directly after exposure for 30 minutes at the age of 14 days (the end of the exposure to the sound of period). Significant improvement (P<0.05) in histological examination at the along of the ganglion in the brain to Movement of Chicken Feet (1), Regular Soft Timid Hens (2), Chicks Care (3) in 42 days.

58 - BASELINE NATURAL KILLER CELL CYTOTOXICITY IS ENHANCED IN THE PRESENCE OF POST-EXERCISE AUTOLOGOUS SERUM

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Keywords: -NKCA, cycling, stress hormones

Natural Killer (NK) cells recognize and eradicate tumor cells. Multiple studies have shown that the killing capacity of each NK-cell (termed Natural Killer Cell Activity(NKCA)) is greatest during recovery from exercise. However, the factors responsible for increased NKCA per cell after exercise are not fully understood. It is thought that exercise-induced phenotypic shifts in NK-cell subsets play a role. Exercise also alters the concentration of various stress hormones(glucocorticoids) and cytokines, which could also impact NKCA. PURPOSE: To determine the role of exercise-induced shifts in NK-cell subsets, cytokines and hormones on exercise-induced changes in NKCA per cell. METHODS: Healthy adults (n=13,7women; 31.9±7yrs) cycled 30min at 115% of their lactate threshold power. Blood was collected pre-, post-, and 1H post-exercise. Effector cells isolated from blood were incubated with K562 or U266 tumor target cells in the presence of autologous serum. NKCA was assessed after 4h by measuring lysed target cells in a flow cytometry based assay. NK cell phenotype was also assessed by 10-parameter flow cytometry. To investigate the effects of hormones and cytokines released during exercise, pre-exercise effector cells were incubated with target cells in the presence of pre-, post-, and 1H post-exercise serum. The effect of shifts in NK-cell subsets was determined by incubating pre-, post- and 1H post-effector cells with target cells in the presence of pre-exercise serum. Linear Mixed Models were used to assess the effect of time and condition on NKCA on a per cell basis and NK-cell phenotype. RESULTS: The cytotoxicity of pre-exercise effector cells was significantly increased against the HLA-expressing target cells(U266) when incubated in 1H post-exercise serum (Pre vs.post vs.1H post =0.318±0.039vs. 0.334±0.039vs. 0.438±0.039,$p<0.05$). Incubation of pre-effector cells with1H post-exercise serum significantly reduced the proportion of cells with the inhibitory phenotype NKG2A+/ NKG2C-(Pre vs.post vs.1H post=45.0±6%vs. 44.2±6%vs. 42.8±6%,$p<0.05$) on NK cells. There was no difference in cytotoxicity of pre-, post-, 1H post-effector cells incubated with pre-exercise serum (Pre vs.post vs.1H post =0.321±0.047vs. 0.282±0.047vs. 0.323±0.047,$p<0.05$). CONCLUSION: The cytotoxicity of resting NK-cells is enhanced following incubation with autologous serum drawn 1H-post exercise. This corresponds with decreased proportion of NK-cells exhibiting the

inhibitory phenotype NKG2A+/NKG2C-. We suggest that exercise-induced changes in serum increase NKCA. Future work will identify the levels of hormone and cytokines that are present in 1H post-exercise serum.

59 - ELDERLY PEOPLE PRACTITIONERS OF A COMBINED EXERCISE TRAINING SHOWS IMPROVEMENT OF SPECIFIC ANTIBODIES IN RESPONSE TO INFLUENZA VIRUS VACCINATION

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Aging process is a multifactorial phenomenon characterized by a decline in many physiological compartments, including the immune system, which is named immunosenescence. Among several changes in the immune response associated with aging there is a greater susceptibility to infection and reduced response to vaccination (1). Although it is widely accepted that regular physical exercise practice, particularly of moderate intensity, can minimize some aspects of immunosenecence (2), the effects of combined exercise training, involving aerobic and resistance physical exercises is poor understood. Therefore, in this study, we evaluated the levels of specific antibodies (IgM and IgG) in response to influenza virus vaccination, TNF-alpha serum concentration and the absolute number of naïve $TCD4^{+}$ cells in elderly people who practice or not a regime of combined exercise training. Thirty-eight elderly individuals [aged = 67.4±5.5), men (n=6) and women (n=32)] were recruited to participate and, afterwards, they were separated in two groups:

sedentary group (SE, n=19, aged = 67.9±6.7) and physical exercise group (PE, n=19, aged = 67.1±4.3). Combined exercise training was composed by aerobic and resistance exercises performed in a moderate intensity. All the volunteers received the same vaccine against influenza virus. Blood samples were collected before and 30 days after vaccination. Both groups presented similar physical characteristics. We observed that PE group presented higher serum IgM and IgG levels after vaccination when compared to the values obtained before vaccination. Furthermore, after vaccination, PE group presented raised serum IgM levels when compared to SE group. Concerning serum TNF-alpha concentration, the values observed in PE group were significantly reduced in comparison to the values observed in SE group. On the other hand, the absolute number of naïve $TCD4^+$ cells in PE group was higher than in SE group. It has been demonstrated that elevation in TNF-alpha levels are related to $TCD4^+$ cells apoptosis, especially naïve T cells (3), leading to the impairment of the immune response to new antigens. Taken together, our results show that elderly people who practice combined exercise training regularly can improve IgM and IgG antibody levels in response to influenza virus vaccination. This effect occurs due to the reduction of serum TNF-alpha concentration and the maintenance of naïve $TCD4^+$ cells number.

60 - PPAR-γ ACTIVATION RESTORES LIVER INFLAMMATION AFTER CHRONIC EXERCISE IN PPAR-α KNOCKOUT OBESE MICE.

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Background: Inflammation has exhibit a straight correlation to nonalcoholic steatohepatitis (NASH). Chronic moderate exercise is one of the main treatments for

NASH by decreasing hepatic pro-inflammatory cytokines and activating PPARs family (1). PPAR-α and γ are the most common isoforms expressed in liver. PPAR-γ plays key anti-inflammatory role decreasing NF-κB activity and promoting M2 macrophages polarization, whereas PPAR-α acts modulating the transcription of enzymes involved in β-oxidation, favoring fatty acid oxidation (2). Obese PPAR-α knockout (KO) mice exhibit low liver lipid accumulation but increases liver inflammation when trained, followed by a reduction in PPAR-γ protein and gene expression (3). So here, we investigated whether rosiglitazone treatment (PPAR-γ activation) could restores liver inflammation after chronic exercise in PPAR-α knockout obese mice**. Methods:** PPAR-α KO mice were fed with high fat diet (HF, 59% fat) during 12 weeks, and allocated in 3 groups: 1) HF-KO (remained sedentary); 2) HFT-KO (submitted chronic moderate training on a treadmill during the last 8 weeks; and 3)HFT-RG-KO (submitted chronic exercise training and had 15mg/kg/day of oral rosiglitazone during the last 8 weeks). We evaluated lipid profile, cytokines (ELISA) and gene expression (RT-PCR) in the liver. **Results:** Rosiglitazone was efficient in reversing PPAR-α knockout mice Insulin resistance and decreased free fatty acid in serum. The protein expression of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α, MCP-1) and NF-κB and IL-1β mRNA were decreased in HFT-RG-KO comparing to HFT-KO indicating low liver inflammation. Although PPAR-γ mRNA were not modified, its target genes (PGC-1α and FAS) where higher to HFT-RG-KO compared to HFT-KO implying PPAR-γ activation. F4/80 expression was reduced in both exercise groups, and CD86 gene expression had a decrease only in HFT-RG-KO suggesting M2 polarization. **Conclusions:** Rosiglitazone treatment was efficient to induce PPAR-γ activation leading to low liver inflammation after chronic exercise in PPAR-α knockout obese mice.

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61 - EFFECT OF LACTIC ACID BACTERIA ON MUCOSAL IMMUNOLOGY AGAINST E.COLI INFECTION IN POULTRY BIRDS

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Keywords: lactic Acid Bacteria, *E.coli*, Mucosa, Macrophages, Migration Inhibition Factor, Mucosal immunology, Cell mediated immune Response.

Poultryis a well-developed sector of agriculture industry in Pakistan. Poultry industry plays a major role in the GDP of Pakistan. Many food borne pathogens play role in causing different digestive problems in poultry and influence the production of eggs and meat. In poultry industry extensive antibiotics are used to control these pathogens for the improvement of meat and egg production. Present study was conducted to evaluate the impact of lactic acid producing bacteria on the immune status against *E.coli* infection in poultry birds. Lactic acid bacteria i.e. *lactobacillus fermentum* was isolated from conventional yoghurt sample. Out of 20 samples 13 samples were positive for *lactobacillus fermentum* which were identified on the basis of their morphological characteristics as it is gram positive rod shaped bacteria with small white round colonies on MRS agar. *Lactobacillus fermentum* was furthered identified on the basis of their biochemical tests as it was catalase negative and different sugar fermentation tests. After identification three concentrations were maintain that were 10^4, 10^5,10^6 cfu/ml. A trial was conducted on the poultry birds.

They were divided into four groups A, B, C and D. Different concentration of probiotics which were Control, 10^4, 10^5and10^6 cfu/ml were given to each group respectively. Birds were kept for 15 days. At day 7 and 15 plasma were collected from respective groups of poultry. At day 10 birds were administered with avian pathogenic strain of *E.coli* (heat inactivated). Macrophages were collected from the peritoneal cavity of poultry birds. Macrophages migration inhibition factor assay were performed invitro. The results of this assay showed that group administered with high probiotic concentration i.e 10^6 cfu/ml showed that immune response was increased more effectively against *E.coli* as compared to other poultry groups. Because % inhibition of macrophages was 64%, 52%, 44% and 31 % for D, C, B and A respectively. The results showed that the group with high % inhibition of macrophages show significantly high cell mediated immune response against *E.coli.*

62 - DIFFERENT EXPRESSION TONES OF CENTRAL AND PERIPHERAL ENDOCANNABINOIDS LEVELS IN OVERWEIGHT AND OBESE MICE

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Keywords: Endocannabinoids; overweight; obesity

Introduction Overweight and obesity are associated with activation of the endocannabinoid system (Silvestri et al., 2011). However, it is not clear whether there is a different expression tone of the endocannabinoids (ECs) between the overweight and obese groups. We assume that endocannabinoids 2-arachidonoylglycerol (2-AG), Anandamide (AEA) and N-oleylethanolamine (OEA) levels are higher in the brain and serum of obese individuals than in overweight groups. **Purpose** To explore the differences of ECs levels in central and peripheral between overweight and obese mice fed on a high fat diet and to analyze the relationship between ECs and body fat ratio. **Methods** C57BL/6J male mice, at four weeks old, were randomly divided into control group (n=25, fed normal diet) and high

fat diet group (n=205, fed D12492, 60% fat) by EXCEL random grouping table. After an 8-week of follow-up, 10 mice were randomly selected from the control group, and their average body weight (BW) was defined as X (g). Then the mice fed on high fat diet were divided into two groups based on their BWs as compared to X: overweight (110-119% X) and obese (120-149% X) group. High performance liquid chromatography (HPLC) were used to detect endocannabinoids levels [including 2-AG, AEA, OEA]. Body fat ratio = (Perirenal and epididymal fat mass)/BW*100%. Data were shown as mean ± standard deviation (SD) and independent t test was used to analyze ECs levels between two groups. $P < 0.05$ was considered to be significant. Results

1) Serum 2-AG, AEA and OEA were higher in obese group (141.55±89.90; 21.54±12.96; 63.44±42.27) than in overweight group mice (116.09±126.91; 19.72±18.96; 43.23±37.15, respectively, unit: pg/ml), although statistical significances were not reached ($P>0.05$, for each comparison); 2) Brain tissue AEA and OEA in obese group (0.43±0.12; 0.68±0.19) were significant higher than overweight group (0.31±0.10; 0.49±0.10; $P<0.05$ and $P<0.01$ respectively, unit: ng/mg); 3) Taken overweight and obese group as a whole (n=20), we found brain tissue OEA showed a positively relationship with BW ($r=0.376$, $P<0.05$) and body fat ratio ($r=0.427$, $P<0.05$). **Conclusion** Central and peripheral ECs show a rising trend as body weight gains and OEA may be more relevant to the increase in fat mass.

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No potential conflicts of interest relevant to this abstract were reported.

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63 - GUT MICROBIOTA IN EXERCISE TRAINED TOLL-LIKE RECEPTOR 5 DEFICIENT MICE INHIBITS FATTY LIVER AND HEPATIC INFLAMMATION

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Keywords: FMT, obese mice, fat accumulation

Introduction: Metabolic syndrome may prove to be the greatest crisis to global healthcare. Recent studies have shown that the pathogenesis of metabolic syndrome is associated with the dysfunction of the gut microbiota. Germ-free or antibiotics based manipulation of the microbiota in mice has been shown to have effects on adiposity, glucose tolerance and inflammation. In contrast, we showed that exercise induced changes in the gut microbiota and inhibition of metabolic syndrome in metabolic syndrome-prone mice, were lacking Toll-like receptor 5 (Tlr5-/-). However, it is unclear whether gut microbiota in exercise trained Tlr5-/- mice is able to inhibit metabolic syndrome in obese mice. Although the idea of transplanting gut microbiota into animals is longstanding, it has never been reported that exercise-induced alterations of microbiota composition enhances host phenotypes. In this study, we investigated the effect of the fecal microbiota transplantation (FMT) from exercise-trained Tlr5-/- mice on metabolic syndrome in obese mice. **Methods:** Male 4-week-old C57BL/6 (wild type: WT, n• • 24) and Tlr5-/- (KO5, n• • 24) donor mice were housed individually in cages with (wheel running: WR, n=12) or without (control: Ctrl, n=12) a running wheel that was accessible 24 hours per day for 20 weeks. After the end of the treatment, the collected cecam was transplanted into the gut of obese recipient mice (male 12-week-old C57BL/6, n• • 48), who were induced by a high-fat-diet (HFD), once per week for three weeks by stomach sonde. **Results:** HFD-induced obesity and glucose intolerance, which are indicators of the metabolic syndrome, occurred in all of the recipient mice. Namely, the difference among the gut microbiota did not affect the host phenotypes. In the liver, however, fat accumulation and mRNA expression of TNF-alpha were attenuated by FMT from KO5 WR mice. Thus, the part of the host phenotypes, which are attenuations of HFD-induced-hepatic dysfunction, can be transmitted for a period of time to recipient mice via transplantation of their gut microbiota.

Conclusion: In conclusion, our results suggest that FMT from exercise trained Tlr5-/- mice might induce low fat accumulation with low grade inflammation in the livers of obese mice.

64 - ALTERED GUT MICROBIOTA BY VOLUNTARY EXERCISE IN DONOR MICE MAY CONTRIBUTE TO HIGH PHYSICAL ACTIVITY IN RECIPIENT MICE

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Keywords: wheel running, cecal microbiota transplantation

Introduction: Recent studies have shown that the changing composition of the gut microbiota is linked with changes in human and animal behaviors, suggesting that behaviors might be regulated via the microbiota-gut-brain axis (Cryan & Dinan, 2012). Although germ-free conditions are associated with increased spontaneous motor activity in mice (Bäckhed, et al., 2007), the mechanisms underlying the relationship between locomotive activity and the gut microbiota of mice are unknown. In the present study, we determined whether the effects of exercise-induced changes in the physical behavior of mice occurred through alterations in the gut microbiota. **Materials & Methods:** Four-week-old male donor C57BL/6 mice were treated to voluntary wheel running (WR) or were kept in a sedentary condition (SED) for 12 weeks, and then the cecal contents were collected. After antibiotic treatment, the cecal microbiota transplantation (CMT) was initiated by placing of the donor cecal contents directly into the oral cavity of recipient mice. These recipient mice were 4-week-old male C57BL/6 mice and had been fed a high-fat diet (HFD). The CMTs were carried out 3 times over a 3-week period (Vijay-Kumar, et al., 2010). The physical activity of all of the HFD recipient mice was examined for 7 days (Swallow, et al., 1998). The physical activity was evaluated by wheel-running activity, which was performed on a wheel adjacent to the cage for 24 hours**. Results & Discussion:** In donor mice, the increases in body mass were attenuated by WR. Moreover, we

observed low body fat and hypertrophy of the heart in WR donor mice. The CMT from WR and SED donor mice did not have an affect on the body, heart and fat mass in recipient HFD mice. Nevertheless, CMT from the WR donor mice into recipient mice induced high physical activity ($p<0.01$). **Conclusion:** These results suggest that gut microbiota transplantation from exercised mice might regulate physical activity in recipient mice.

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65 - EFFECTS OF GLUTAMINE SUPPLEMENTATION ASSOCIATED WITH MODERATE EXERCISE IN NEUTROPHILS FUNCTION IN ELDERLY WOMEN

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Keywords: CD 62L, phagocytosis, reactive oxygen species, cytokine, maltodextrine supplementation.

Aging changes the immune system as well as most physiological functions. Neutrophils are innate immune cells and are known as the body´s first line of defense against infection and inflammation. Studies demonstrated that neutrophil functions can be altered by aging, thus strategies to prevent these losses have been studied. Glutamine and exercise are modulators of neutrophil function, but there are no studies in the literature on their effects on the elderly. The objective of the present study is to evaluate the effect of chronic supplementation with maltodextrin associated with glutamine on the neutrophil function from active and elderly women practicing supervised moderate physical exercise. Fourty five healthy elderly volunteers, aged between 60 and 80 years, were grouped into two groups: Control (Active) (n = 24) and Exercise (n = 21). These groups were subdivided into 2 supplemented groups: Maltodextrin (M) receiving 20 g of Maltodextrin / day and Glutamine-associated maltodextrin (MGln) group which disrupted 10 g of L-glutamine + 10 g of maltodextrin / day, both diluted in 250 ml of water. Peripheral blood sample were collected before and after chronic supplementation performed for 30 days. The following neutrophil functions were evaluated: expression of the CD62L adhesion molecule, migration using transweel plate; Phagocytosis by quantification of the ingestion of opsonized zimozan particles; Intra and extracellular production of reactive oxygen species (ROS) by luminescence assay using lucigenin and intracellular production of ROS by flow cytometry. In addition, cytokine production was also determined using the CBA (Cytometric Bead Array) method by flow cytometry. The data were analyzed using software SPSS version 20, non-parametric test Kruscal Wallis, as well as R for differentiation between pairs, considering a level of significance of 95%. MGln supplementation increased CD62L expression in the Exercised Group comparing to Control, and increased IL10 production by neutrophils

stimulated with LPS; the pro inflammatory cytokines were not changed after MGln supplementation. On the other hand, supplementation with M increased IL-1β production (224.3%) in the Exercised Group comparing to Control and increased IL-8, TNF-α and IL6 production by neutrophils stimulated with LPS. The ROS production intracellular (157.3%) and extracellular (169%) was also increased in neutrophils from Exercise Group supplemented with MGln comparing to Exercise Group supplemented with M. We concluded that supplementation with MGln prevented the increase of the inflammatory cytokine production and stimulated neutrophil function only in the elderly women practicing moderate supervised exercise.

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66 - INCREASED MACROPHAGE INFILTRATION AND TNF-α LEVELS IN THE ADIPOSE TISSUE OF OBESE ZUCKER RATS AFTER HABITUAL EXERCISE-INDUCED STRESS

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Keywords: obesity, exercise, stress, TNF-α, macrophages

Metabolic syndrome (MS) is a disorder associated with obesity and constitutes a risk factor for type-2 diabetes mellitus and a state of “low grade inflammation”. The main molecular link between inflammation and obesity is TNF-α. This pro-inflammatory cytokine has been reported to be over-expressed and over-produced in the adipose tissue of rodent models of obesity, and it is also involved in insulin resistance. The sources of this cytokine are mainly macrophages that invade the adipose tissue in

obese individuals. Regular moderate exercise is a good non-pharmacological therapeutic strategy in the management of MS since it improves diabetic status, insulin sensitivity, and the immune response. Based on the potential anti-inflammatory effects of exercise, it has been also proposed as a good strategy to control low-grade inflammation. Nevertheless, exercise can also elicit a danger-stress and inflammatory response that may become detrimental to health. Thus, in previous studies we found that an exercise of an inappropriate intensity worsened the dysregulation in the feedback mechanisms between the inflammatory and stress responses in the obese Zucker rat model of the metabolic syndrome, even increasing the systemic concentration of glucose. In the present study we have hypothesized that a program of habitual exercise-induced stress (running, 5 days/week for 35 min at 35 cm/s for 14 weeks) could also contribute to increased infiltration of macrophages and to increased levels of TNF-α in the adipose tissue of obese Zucker rats (fa/fa), which may contribute to the systemic hyperglycemia. Infiltrated macrophages and TNF-α expression in the white adipose tissue was determined by lectin histochemistry and immunohistochemistry; noradrenaline (NA) by HPLC, and glucose by standard method. The adipose tissue from obese sedentary rats showed higher levels of infiltrated macrophages and TNF-α than those observed in lean rats (Fa/fa) as reference values. The program of exercise increased the number of infiltrated macrophages and the expression level of TNF-α in the adipose tissue of obese rats, together with an increase in the circulating NA and glucose concentrations. Thus, the intensity of this program of habitual exercise could be considered as an example of “dangerous exercise”. It is concluded that inadequate exercise-induced stress can further increase the obesity-induced augmented infiltration of macrophages and the TNF-α overexpression in the adipose tissue of obese animals, thus contributing to the metabolic, inflammatory, and stress disorders associated with the metabolic syndrome.

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67 - β2 ADRENERGIC REGULATION OF THE PHAGOCYTIC ACTIVITY OF MONOCYTES IN OBESE MICE: EFFECT OF AN ACUTE INTENSE EXERCISE

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Keywords: acute exercise, adrenergic receptor, obesity, phagocytosis

Obesity is a worldwide epidemic and it is associated with comorbid conditions that involve alterations of the innate/inflammatory immune response. Obesity is also correlated with changes in the activity of the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis. Catecholamines are important immunoregulatory molecules, and adrenergic agonists interfere with the inflammatory response. On the other hand, physical activity, besides activating the SNS and HPA axis, is an event that can reverse pathologies arising from obesity (Ortega et al., 2015). However, the influence of obesity on the adrenergic regulation of the immune system, and the influence of exercise on the mechanisms underlying this regulation in obesity, is still not well understood.

The aim of this study was to investigate the influence of obesity and the effects of a single bout of acute exercise (running, 35 min at 16 m/min) on the β_2 adrenergic regulation of the phagocytic capacity of monocytes. A group of 20 ten-week old C57BL/6J mice were fed a diet containing either 5% (lean group, n=10) or 40% of fat –60% of the kcal from fat– (obese group, n=10) for 18 weeks. Then, 5 animals from each group were subjected to the acute exercise. The monocytes´ phagocytic capacity was evaluated by flow cytometry in whole blood collected by cardiac puncture, in the presence or absence of the β_2 adrenergic agonist terbutaline.

First, obese mice showed a lower phagocytic monocyte percentage than lean mice, and the acute exercise decreased the phagocytic monocyte percentage (mainly in lean mice) and increased their phagocytic activity in both groups. Terbutaline decreased the phagocytic percentage in both lean and obese mice, but it did not change the phagocytic activity. However, animals that performed the bout of acute

exercise (both lean and obese), presented an increased phagocytic activity in response to terbutaline.

To conclude, it seems that, although there was an overall lower phagocytic capacity of monocytes in obesity, both obese and lean mice showed a similar response to acute exercise and a similar β_2 adrenergic regulation of phagocytosis. However, this β_2 adrenergic regulation seemed to be different after acute exercise than at rest, since the β_2 adrenergic stimulation induced an increased phagocytic activity only during acute exercise.

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68 - β2 ADRENERGIC REGULATION OF THE PHAGOCYTIC ACTIVITY OF PERITONEAL MACROPHAGES IN OBESE MICE: EFFECT OF AN ACUTE INTENSE EXERCISE

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Keywords: acute exercise, adrenergic receptor, obesity, phagocytosis.

Obesity is a worldwide epidemic and it is associated with comorbid conditions that involve alterations of the innate immune response. It is also correlated with changes in the function of the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis. Catecholamines secreted by the SNS and the adrenal glands are important immunoregulatory molecules, and adrenergic agonists interfere

with the inflammatory response. In addition, exercise, besides activating the SNS and HPA axis, is an event that can reverse pathologies arising from obesity (Ortega et al., 2015). However, the influence of obesity on the adrenergic regulation of the innate immune response, and the role of physical activity on the mechanisms underlying this regulation in obesity, are still not well understood.

The aim of this study was to investigate the influence of obesity, and the effects of a single bout of acute exercise (running, 35 min at 16 m/min) on the β_2 adrenergic regulation of the phagocytic capacity of peritoneal macrophages. A group of 20 ten-week old C57BL/6J mice were fed a diet containing either 5% (lean group, n=10) or 40% of fat –60% of the kcal from fat– (obese group, n=10) for 18 weeks. Then, 5 animals from each group were subjected to the acute exercise. The macrophages´ phagocytic capacity against opsonized bacteria was evaluated by flow cytometry in peritoneal macrophages, in the presence or absence of the β_2 adrenergic agonist terbutaline.

The results showed a lower phagocytic macrophage percentage in the obese mice than in the lean mice. Acute intense exercise decreased the phagocytic percentage and increased the phagocytic activity of macrophages in both groups. In addition, terbutaline seemed to decrease the phagocytic percentage and phagocytic activity of macrophages in both groups, irrespective of performing exercise or not.

In conclusion, these results suggest that obesity presents a deteriorated phagocytic capacity of peritoneal macrophages, probably contributing to an impaired defence against bacterial infections. The exercise-induced decrease in the percentage of the phagocytic macrophages seems to be compensated by an increased activity of these cells, irrespective of obesity. The activation of β_2 adrenergic receptors seems to decrease the phagocytic capacity of macrophages, irrespective of weight and of performing exercise or not.

This investigation has been supported by “Ministerio de Economía y Competitividad” (DEP2015-66093-R). We would like to thank the STAB (UEx) for technical and human support.

Ortega, E., Martín-Cordero, L., García-Roves, P.M., Chicco, A.J., González-Franquesa, A., Marado, D. (2015). Diabetes Mellitus and Metabolic Syndrome. In: Palavra, F., Reis, F., Marado, D., Sena, A. ed. Biomarkers of Cardiometabolic Risk, Inflammation and Disease. Switzerland: Springer International Publishing, pp. 55-79

69 - EFFECT OF EXAM PERIODS ON PHYSICAL ACTIVITY AND THE IMMUNE-NEUROENDOCRINE RESPONSE IN UNIVERSITY STUDENTS

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Keywords: Phagocytic process, neutrophils, stress, cortisol, sedentary lifestyle

Living a healthy lifestyle is crucial in order to prevent numerous diseases. Lifestyle is affected by several factors such as eating habits, toxic habits, physical activity, sleep patterns and psychological factors. In particular, physical activity is a major health determinant. Nowadays, sedentary lifestyle and physical inactivity are considered a worldwide health problem (Blair, 2009).

The purpose of this study was to analyze how exam periods may affect physical activity and immune-neuroendocrine parameters in young university students. A group of 8 healthy students from 19 to 26 years in age were enrolled in the study. Anthropometric measurements (weight, body mass index and waist-hip ratio) were taken using standardized methods. Daily physical activity and the Metabolic Equivalent of Task (MET) were measured using accelerometers (ActiGraph wGT3X-BT) for 4 days. Fasting plasma glucose levels were determined using blood glucose strips, and cortisol serum levels were measured by ELISA. The phagocytic process was evaluated in neutrophils from peripheral blood. Chemotaxis was evaluated in isolated neutrophils using a Boyden chamber, and the phagocytic and microbicide capacities were evaluated in whole blood by flow cytometry. Evaluation of all of these parameters was carried out both in the exam period and in the post-exam period.

During the exam period, the students presented a higher weight and body mass index. They performed less and shorter bouts of activity, less minutes of moderate-to-vigorous intensity physical activity and fewer steps than after exams. Students during exams also showed lower MET values, decreased glucose levels, and higher

cortisol levels. During the exam period, students presented a reduced chemotaxis index, and decreased phagocytic and microbicide capacities of neutrophils; which may suggest a suppression of the immune system´s defenses against pathogens. Taken as a whole, these results clearly suggest that the exam period deeply affected lifestyle since it had a significant impact on different aspects of the students' health such as physical activity, anthropometric measurements, and immune and endocrine parameters. Nevertheless, despite the improvement in physical activity in the post-exam period in relation to the exam period, both situations reflect worrying high levels of physical inactivity that may contribute to the onset of sedentary lifestyle-related pathologies in the future.

This investigation has been supported by Junta de Extremadura-FEDER (GR-15041). We would like to thank the volunteers and the STAB (UEx) for technical and human support.

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70 - A COMPARATIVE STUDY OF PHYSICAL ACTIVITY AND THE INNATE IMMUNE RESPONSE BETWEEN YOUNG AND AGED UNIVERSITY STUDENTS

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Keywords: Aging, sedentary lifestyle, phagocytic process, stress

The base of the functional longevity of each individual is health maintenance. This depends mainly on the lifestyle and environmental factors, thus it is possible to retard the rate of ageing through the modulation of these factors. Lifestyle is affected by factors such as eating habits, toxic habits, sleep patterns or physical activity. It has

been demonstrated that the competence of the immune system is an excellent marker of health, and habitual exercise is an important approach to improve the immune system, especially in old people (De la Fuente et al., 2011).

Thus, the aim of this investigation was to evaluate the daily physical activity performed by old and young university students, together with their immune and neuroendocrine response. 8 healthy young university students (University of Extremadura) from 19 to 26 years in age were compared with 8 healthy elderly university students (Elderly People´s University of the University of Extremadura) from 63 to 71 years in age. Anthropometric measurements (body mass index and waist-hip ratio) were taken using standardized methods. Physical activity and the Metabolic Equivalent of Task (MET) were measured using accelerometers (ActiGraph wGT3X-BT) for 4 days. Fasting plasma glucose levels were determined using blood glucose strips, and cortisol serum levels were measured by ELISA. Chemotaxis of isolated neutrophils from peripheral blood was evaluated using a Boyden chamber. The phagocytic and microbicide capacities of monocytes and granulocyteswere evaluated in whole blood by flow cytometry.

The aged volunteers presented a higher body mass index, waist-hip ratio, and glucose values; but no differences in cortisol levels were found. Surprisingly, the elderly group performed higher daily physical activity levels: more minutes of moderate-to-vigorous physical activity, more steps, and greater MET values than the younger group. Moreover, they showed a better neutrophils' chemotaxis capacity and a better monocytes' microbicide capacity than the young students; thus indicating that the elderly students did not present an innate immunosenescence status.

These results may reflect worrying high levels of physical inactivity in young people. In addition, this may contribute to decrease the immune system´s defenses against pathogens, and also to compromise health maintenance and favour the onset of sedentary lifestyle-related pathologies in the future.

This investigation has been supported by Junta de Extremadura-FEDER (GR-15041). We would like to thank the volunteers and the STAB (UEx) for technical and human support.

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71 - EXPLORING POTENTIAL IMMUNE SYSTEM MARKERS FOR PREDICTING FRAILTY SYNDROME IN OLDER ADULTS: DIFFERENT STATISTICAL APPROACHES

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Keywords: Frail older adults, Immune system, Classification algorithms, geriatric assessment.

Background: The early identification of older populations with an increased risk for frailty syndrome (FS) is one of the most important goals for geriatricians[1]. **Goals:** We aim to assess how different machine learning procedures may be applied to accurately predict FS by testing different immune system markers (ISM) as putative predictors**. Methods:** A group of 110 institutionalized-dwelling participants (94 females and 16 males; mean age = 82.0±7.8 years old) were assessed for frailty using the Fried's FS protocol[2] with 48 being found to be frail and 62 to be non-frail or pre-frail. Twelve blood and salivary ISM were determined by ELISA. Both univariate (receiver operating characteristics, ROC) and multivariate (machine learning) analyses were performed to assess the contribution of the different predictors. **Results:** Only three variables were seen to have statistically significant diagnostic values in the ROC analysis: testosterone, with area under the curve (AUC), sensitivity and specificity equal to 0.63, 66.7% and 59.7%, respectively; α-amylase (0.64, 64.6% and 64.5%) and IL-6 (0.63, 87.5% and 41.9%). Gini coefficients were computed to sort out the relative importance of the number of predictors (m) and allow for a variable reduction strategy. By decreasing order of importance, the latter were: Testosterone, α-amylase, IL-6, Cortisol, IgA, DHEA, CRP, TNF-α, Lysozyme, IL1-b, IL-10, IFN-g. The m most relevant predictors (m ranging from 1 to 8) were

taken to build up classification models with Logistic Regression (LR), Support Vector Machines (SVM) and Random Forests (RF) models, which were implemented in R 3.3.2. The models were assessed using Monte Carlo cross-validation with 500 random splits of the data into training and test sets[3]. For each split, 70% of the data was assigned to the training set. In terms of AUC attained, once again determined by using ROC analyses, the best models were obtained with RF using 8 predictors: Testosterone, α -amylase, IL-6, Cortisol, IgA, DHEA, CRP, TNF-α. The corresponding 95% confidence intervals for the AUC, sensitivity and specificity were [0.71; 0.76], [0.70; 0.77] and [0.70; 0.77], respectively. **Conclusion:** Models with solely 8 ISM predictors display a promising diagnostic value for a standard immunological screening tool for FS.

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72 - IMMUNOPROTECTIVE ACTION OF IRISIN – STUDY ON MACROPHAGE RAW 264.7

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Keywords: irisin, anti-inflammatory activity, exercise, macrophage, immune defense

Irisin, an adipomyokine secreted mainly by skeletal muscles and by adipocytes, is intensively studied since its re-discovery by Boström et al. in 2012 in the new context as ´an exercise hormone´ [Erickson, 2013]. Due to an increase of circulating irisin level during physical exercise, it is referred to as the mediator of physical activity [Moreno et al., 2015].A growing number of studies indicated its potentially protective action in some metabolic disorders, including obesity-related diseases [So et al., 2014]. The aim of the present study was to determine the impact of irisin on inflammation generated by macrophages. Different concentrations of irisin (0 - 100 nM) were applied to assess the activity of quiescent and lipopolysaccharide (LPS)-activated murine RAW264.7 macrophages in apoptotic and viability tests as well as migration and adhesion assays. The study analyzed also irisins effect on the expression and secretion of oxidative stress mediators and pro-inflammatory cytokines released by macrophages. The results showed that irisin, by reduction of reactive oxygen species (ROS) and enhancement of heme oxygenase 1 (HMOX-1), and catalase 9 (CAT-9) levels, protects against oxidative stress in a dose-dependent manner. The anti-inflammatory potential of irisin includes the ability to impair macrophages migration via regulation of expression and release ratios of matrix metalloproteinase-9 (MMP-9) and its tissue inhibitor (TIMP-1). The biological activity of irisin, mediated through the TLR4/MyD88 signaling pathway, results in attenuation of the mitogen-activated protein kinases (MAPKs) and phosphorylation of nuclear factor kappa B (NFkB) and finally reduction of pro-inflammatory cytokines expression and secretion, including tumor necrosis factor (TNF), interleukin 1 and 6 (IL-1a, IL-6), C-X-C motif chemokine ligand 1 (CXCL1), monocyte chemoattractant protein-1 (MCP-1) and high mobility group box-1 protein (HMGB1).

Our study clearly demonstrated that irisin is a promising molecule for the anti-inflammatory treatment of macrophages. In addition to obvious health benefits of regular physical activity, also by modulation of the immune system, we showed that irisin is involved in the reduction of macrophage pro-inflammatory activity and protection from oxidative stress generated by these immune cells.

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73 - TNF-α PRODUCTION IN LPS-STIMULATED WHOLE BLOOD CULTURES IN OBESE ADULTS IS DECREASED AFTER 3-WEEK OF HIGH-INTENSITY INTERMITTENT TRAINING

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Introduction: Obesity is characterized by pro-inflammatory condition, with high levels of tumor necrosis factor – alpha (TNF-α) especially released by macrophages and monocytes (CD14) pathway lypopolysaccharide (LPS) from Gram-negative bacteria-binding to receptor Toll-like receptor 4 (TLR4). The excess of TNF-α can trigger insulin resistance that increases lipolysis, leading to accumulation of free fatty acids in the bloodstream, which can induce cardiovascular diseases. Exercise has been effective to decrease both TNF-α and TLR4 independently of weight loss. However, it is not known if the intensity of exercise can influence this response. **Aim:** To compare the effectiveness of two different types of aerobic exercise performed during three weeks in the production of TNF-α stimulated by LPS in whole blood in response to short-term training. **Methods:** 12 sedentary obese men (age: 30.9±5.1 years; BMI: 35.2 kg/m^2; VO_{2peak}: 36.26±4.9 mL/kg/min) were randomized into two different groups with isocaloric training protocols (291.5±32.8 Kcal): HIIT (10 bouts of

1-min at 100% VO_{2peak}: 1-min passive recovery) or moderate intensity continuous training (MICT) at 65% VO_{2peak}. Blood samples were collected after overnight fasting at baseline and after three weeks. We used whole blood in short time (1h) LPS-stimulated cultures for analyses of TNF-α levels. Independent t-test compared delta percentages (Δ%) of blood samples in HIIT and MICT. **Results:** We found an effect between groups regarding Δ% of TNF-α (HIIT versus MICT: -27.8±25.8 versus 47.3±63.8; t=2.466; p=0.033). **Conclusion:** HIIT (but not MICT) was able to decrease levels of TNF-α after nine sessions of isocaloric exercise. This finding could be explained by different intensities of exercise, since the organism is trying to adjust to the new metabolic stimuli.

74 - EXERCISE TRAINING MODULATES PERITONEAL MACROPHAGES AND ADIPOSE TISSUE MACROPHAGES POLARIZATION INDEPENDENT PPAR-γ

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Background: Exercise training induces anti-inflammatory status in several cells, principally in peritoneal macrophages, and more recently was verified in adipose tissue macrophages. Peroxisome proliferator-activated receptor gamma (PPAR-γ) is speculate to be key transcription factor involved in anti-inflammatory responses mediated by exercise training, however, this hypothesis is yet not evaluates. We aimed to assess the effects of PPAR-γ deletion in macrophages (principally peritoneal and adipose tissue) in animals sedentary and trained. **Methods:** two animal strains were used: CreLox for PPAR-γ (KO) in myeloid cells and C57BL/6 control animals (WT). Each genotype was divided into 2 subgroups 1) sedentary; (WT or KO) 2) trained (WTT or KOT). The experimental protocol lasted 8 weeks (5 times per week for 60% of maximum speed). Flow cytometer of peritoneal

macrophages and Gating strategy used to identify myeloid-cell subsets in the subcutaneous adipose tissue. **Results:** Exercise training was able in promotes M2 macrophages polarization in peritoneal and adipose tissue. However, deletion of PPAR-γ was not able in abolished this response mediated by exercise training. **Conclusion:** Exercise training leads for anti-inflammatory status in peritoneal macrophages and adipose tissue macrophages in mice independent of PPAR-γ.

75 - EFFECT OF SIX WEEKS OF HMB SUPLEMENTATION ON BODY COMPOSITION, BLOOD CHEMISTRY, LIPID PROFILE AND BLOOD COUNT IN PHYSICAL ACTIVE YOUNG MEN

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Keywords: β-hydroxy-β-methylbutyrate, HDL, lean body mass, blood cells, immunology

Abstract

β-hydroxy-β-methylbutyrate (HMB) is a leucine metabolite produced from α-ketoisocaproic acid. HMB supplementation has been used as a dietary supplement in sports since 1997, with the aim of decreasing muscle proteolysis. Because of this it has been propose that HMB could improve body composition and decrease muscle damage.

There are several hypothesis about HMB mechanism of action such as: the increasing muscle cholesterol synthesis, positive effects on muscle metabolism

through both the mTOR and ubiquitin-proteasome pathways, between others. However, there is few research about its effects in blood chemistry and blood count; they bout are related to muscle repair, which is regulated by the immune system.

The aim of this research was compare differences between treatments (placebo and HMB) to know differences in body composition (DEXA), blood chemistry, lipid profile, and blood count of physical active young men having HMB supplementation (3 g / day) or placebo during 6 weeks. They were determinate before and after six weeks of HMB supplementation: body composition (DEXA), blood chemistry, lipid profile, and blood count

After six weeks of HMB supplementation (3 g / day) there were no changes in body composition, blood chemistry, lipid profile, and blood count.

In conclusion, 6 week of HMB supplementation has not shown improve body composition, blood chemistry, lipid profile, and blood count in physical active young men.

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76 - THE INFLUENCE OF AN ACUTE EXERCISE BOUT ON MONOCYTE PHENOTYPE AND CIRCULATING PLATELET-MONOCYTE COMPLEXES IN FIT INDIVIDUALS

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Keywords: platelet-monocyte complexes, monocyte phenotype, acute exercise, inflammation

Purpose: The purpose of this study was to examine the distribution of three monocyte phenotypes and the formation of platelet-monocyte complexes (PMC) following an aerobic exercise bout. **Methods:** Apparently healthy men and women (n=7, age=22.9 ± 5.1) performed a 20 min treadmill run at 85% heart rate maximum followed by five min rest and a maximal graded treadmill test (VO_2max=50.3 ± 8.4 ml×kg^{-1}×min^{-1}). Blood was obtained pre- exercise (PRE), immediately post-exercise (PO) and at 1hr and 2hr post-exercise (1HR-PO and 2HR-PO). In addition, each subject performed a control trial on a separate day by resting in the lab. Blood was collected at the same time points as the exercise trial to control for diurnal variation. Subjects did not exercise for the 36 hours prior to all testing. PMCs and monocyte phenotype were identified via flow cytometry (FACSCelesta, BD Biosciences). Monocyte phenotypes were categorized by the following cell surface receptors: Classical (Mon1) (CD14+CD16−CCR2+), Intermediate (Mon2) (CD14+CD16+CCR2+), and Non-classical (Mon3) (CD14^{lo}CD16++CCR2−). Mon4 was defined as all CD16+ monocytes (both Mon2 and Mon3). All events positive for both CD14 and CD42a (a receptor on platelets) were considered platelet-monocyte complexes. **Results:** As anticipated, exercise induced leukocytosis immediately post-

exercise (EX: PRE=5.74±0.62, PO=8.63±0.90; CON: PRE=5.98±0.61, PO=5.64±0.54 x10^6 cells×ml^{-1}; p=0.045) and at 2HR-PO (EX: 2HR-PO=8.50±0.37; CON: 2HR-PO=6.643±0.55 x10^6 cells×ml^{-1}; p=0.013) compared to the control trial. In addition, the number of circulating platelets increased PO exercise (240± 10.3 vs. 287± 22.3 x10^6 cells×ml^{-1}, p=0.045). The percentage of circulating Mon2 monocytes increased 1HR-PO exercise (15.1±4 vs. 19.6±8.3 %, p=0.050) compared to the control trial. In addition, Mon2 monocytes decreased at the 1HR timepoint in the control trial, most likely due to diurnal variation (17±2.8 vs. 3.4±2.2 %, p=0.026). Mean fluorescence intensity (MFI), a measure of cell receptor density, of CD16 decreased on all CD14+ monocytes (EX: PRE=13,903±2266, 2HR-PO=5845±521; CON: PRE=10,888±2619, 2HR-PO=13704±3017;p=0.027) and on all CD16+ monocytes (Mon4) (EX: PRE=16,999±2840, 2HR-PO=6775±683; CON: PRE=13,814±3654, 2HR-PO=20,126±5346; p=0.033) in the exercise condition compared to the control condition. No significant changes in the percentage of circulating PMCs (PRE=9.67±2.18, PO=9.57±1.22, 1HR-PO=10.39±0.99, 2HR-PO=8.76 %, p>0.05) or the number of PMCs (PRE=2.64±0.63, PO= 4.06±1.25, 1HR-PO=2.79±0.38, 2HR-PO=2.83±0.60 x10^6 cells×ml^{-1}, p>0.05) were observed despite increases in platelet number post-exercise. **Conclusion:** Despite shifts in monocyte phenotype and platelet number, acute exercise did not appear to have an impact on the formation of PMCs in apparently healthy, fit individuals. This is in contrast to previous findings which show increases in PMC formation immediately post-exercise and decreases in PMC formation at 1HR post-exercise. However, previous findings were in older, often untrained or diseased adults and/or the exercise intensity was not as strenuous as that employed here.

77 - SELF-REPORTED MODERATE-HIGH INTENSITY PHYSICAL ACTIVITY DOES NOT REDUCE INFLAMMATORY MARKERS IN OVERWEIGHT/OBESE INDIVIDUALS

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Keywords: obesity, inflammation, Il-17, IL-23, IL-12

Purpose: Obesity-associated systemic inflammation is a major cause of type 2 diabetes, various cardiovascular diseases (CVD), and increased mortality rates. Overweight and obese individuals who are physically active ("fat but fit"), appear to have a similar risk of CVD as do normal weight individuals who are inactive. Physical activity, therefore, is a key mechanism through which metabolic inflammation is reduced. The purpose of this study was to examine the effects of physical activity on circulating inflammatory mediators of cardiovascular disease (IL-17, IL-12, IL-23, IFN-g, L-selectin) in "fit" vs. sedentary overweight/obese individuals.

Methods: Thirty-one overweight or obese (BMI 34.2 ± 5.1 $kg \times m^{-2}$, % fat 40.6 ± 6.7), male and female volunteers aged 35-55 years (44.5 ± 4.8 yrs, 39% males) were categorized into one of two groups based on a validated physical activity questionnaire: sedentary (SED, N= 17, 27 ± 6$ml O_2 \times kg^{-1} \times min^{-1}$) or physically active (PA, N=14, 30 ± 6 $ml O_2 \times kg^{-1} \times min^{-1}$). PA participated in ≥ 180 minutes of moderate-high intensity exercise per week for a minimum of 4 months, including aerobic training, resistance training, or a combination of both. SED participated in structured physical activity ≤ 1 hour per week. Preliminary testing consisted of anthropometric measurements (height, weight, waist to hip ratio), and body composition using dual energy x-ray absorptiometry (DEXA). Maximal oxygen consumption was assessed on a treadmill using the ParvoMed Metabolic measurement system (Sandy, UT). Blood samples were obtained in the fasted (at least 10 hr) state, after subjects

refrained from exercise for 36 hours. Plasma or serum samples were analyzed using an enzyme-linked immunosorbent assay (ELISA) kit (Interleukin-17 (IL-17)), interferon-gamma (IFN-g) (Invitrogen, Carlsbad,CA) or milliplex assay (interleukins 12, 23 (IL-12, IL-23) and L-selectin; EMD Millipore, Billerica, MA) using manufacturer instructions. Hemoglobin A1c was assessed by LabCorp (Fort Worth, TX).

Results: HbA1c (%) was significantly lower in physically active (PA) individuals when compared to the sedentary group (5.5 ± 0.1 vs. 5.8 ± 0.1%, respectively; p=0.031). There were no differences between the groups (PA vs. SED) in any of the inflammatory markers measured (p>0.05). IL-12 was significantly correlated with IL-17 (r=0.647, p<0.0001), IL-23 (r=0.493, p=0.005), and L-selectin (r=0.564 p=0.001). Similarly, IL-17 was positively correlated with L-selectin (r=0.410, p=0.022).

Conclusion: While moderate-intense PA lowered HbA1C %, indicating better carbohydrate metabolism, the *ad libitum* exercise dosage of the "fit" group was not sufficient to successfully decrease low-grade systemic inflammation as measured by the markers here. Further study of well-controlled exercise dose will be necessary to define the minimum exercise dose required to confer tangible health benefits as well as maximize overall health outcomes.

The University of Newcastle, Australia Travel Awards for Early Career Researchers

CANDICE COLBEY

Griffith University, Queensland, Australia

Candice is a PhD candidate in the School of Medical Science at Griffith University, Australia and is a member of the Stay Healthy initiative coordinated by the Australian Institute of Sport. The Stay Healthy project examined environmental and genetic determinants of health in association with the illness and injury status of athletes in preparation for the 2016 Rio Olympic Games. Under the Stay Healthy umbrella Candice's focus is to examine the association between immune regulation, exercise and upper respiratory symptoms. Her thesis adopts a systems level approach that stems from the availability of modern, high-throughput techniques; the application of such methods is currently novel in an exercise immunology setting. She anticipates that this methodology will deliver a comprehensive assessment of long-term immune regulation in response to the demands of elite athlete status. Candice has a Bachelor of Health Science (Class 1 Honours) from Griffith University. Her honours thesis examined immune regulation across the health and disease spectrum, spanning endurance athletes through to overweight and obesity. Her research interests include immunometabolism, the gut microbiota, bioinformatics and nutritional intervention and supplementation for athletic performance. She is particularly excited about contributing to emerging research in the areas of gut microbiota and immunometabolism.

DR NAROA ETXEBARRIA

University of Canberra, ACT, Australia

Dr Naroa Etxebarria is course convener for the Master of High Performance - Sport and Exercise Sciences at the University of Canberra, Australia. Dr Etxebarria has a PhD in 'Physiology and performance of cycling and running during Olympic distance triathlon'. She has held positions in elite athlete support at the Australian Institute of Sport, English Institute of Sport, and various national sporting

organisations. Dr Etxebarria lectures in the biochemistry of exercise and related undergraduate and postgraduate level courses focusing on high performance sport. She also supervises PhD, Masters and honours students at the University of Canberra. A particular focus is the development, evaluation and application of endurance sport and exercise science to inform coaching practice and sports science support to enhance performance. Current research activities include optimisation of short-term heat acclimation, characterisation of sport demands and implementation of training strategies for endurance sports, and gut permeability and health in athletes.

RHIANNON SNIPE

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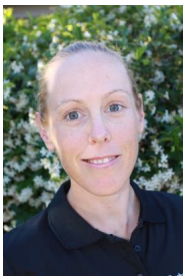

Rhiannon Snipe is a Sports Dietitian currently completing the final year of her PhD with the Monash University Department of Nutrition, Dietetics and Food in Australia. Rhiannon enjoys running marathons but dislikes the gastrointestinal disturbances that commonly affect her training and races. Her sensitive gut has led her towards research in this area. Rhiannon's PhD studies aim to comprehensively investigate the effects of exertional heat stress on gastrointestinal perturbations and subsequently identify nutrition-related prevention and management strategies. She was awarded a Sports Medicine Australia research grant for her study investigating the effects of beverage temperature on the gastrointestinal system during exertional heat stress. On completion of her PhD, Rhiannon aspires towards a career in academia; whilst also pursuing further research in exercise gastroenterology, continuing to assist endurance athletes to resolve their gastrointestinal issues and lowering her personal best time for the marathon.