

BIOSKETCH

Curtis C. Harris, MD

Chief, Laboratory of Human Carcinogenesis, CCR, NCI, NIH

EDUCATION

University of Kansas B.A. 1965 Zoology
University of Kansas School of Medicine M.D. 1969 Medicine

PROFESSIONAL EXPERIENCE

1964-1965 Undergraduate Teaching and Research Assistant, Department of Zoology, University of Kansas
1969-1970 Intern, Department of Medicine, UCLA Hospital, Los Angeles, CA
1970-1972 Research Associate, Lung Cancer Unit, OASDC, DCCP, NCI, NIH, Bethesda, MD
1972-1975 Head, Ultrastructure Unit, Pathogenesis Sect., Lung Cancer Br., DCCP, NCI, NIH
1973-1976 Resident and Trainee in Clinical Oncology, NCI-VA Oncology Branch, Department of Medicine, VA Hospital, Washington, DC (4 months per year)
1975-1981 Head, Human Tissue Studies Sect., Lab. of Exper. Pathol., DCCP, NCI, NIH
1979-1981 Associate Chief, Laboratory of Experimental Pathology, NCI, NIH
1981-Pres. Chief, Laboratory of Human Carcinogenesis, CCR, NCI, NIH, and Head, Molec. Genetics and Carcinogenesis Section

HONORS

1984 Fellow, American Society of Clinical Investigation
1992-95 Member, Board of Directors, American Association of Cancer Research
1995 Deichmann Award and Keynote Lecture: VII International Congress of Toxicology
1995 Walter Hubert Award: British Association for Cancer Research
1996 International Keynote Lecturer, Japanese Surgical Society Annual Meeting
1996 Lewis M. Schiffer Memorial Award and Lecturer, Cell Proliferation Society
1996 Bob Champion Award and Lecturer, British Oncological Association
1997 Keynote Address: AACR-IARC Conference, Molecular Epidemiology
1997 Elizabeth and James Miller Distinguished Lecturer, Rutgers University
1997 Keynote Address: Genes and Environment in Cancer, Dr. Mildred Stiftung FDN
1998 Distinguished Lectureship, Japanese Foundation for Cancer Research, Tokyo
1998 Keynote Address: Latin-Amer. Mtg., Environmental Mutagenesis, Carcinogenesis and Teratogenesis, Curitiba
1999 Charles Heidelberger Award and Keynote Lecturer, Intl. Soc. on Gastroenterological Carcinogenesis, Ulm
1999 Distinguished Service Medal, highest award of the U.S. Public Health Service
2000 Keynote Address: Molecular Epidemiology International Conference, Lyon
2001 Honorary Member, Japanese Cancer Association

- 2001 Gerald Wogan Lecturer, MIT, Boston
- 2002 Award of Merit, Princess Takamatsu Cancer Research Foundation
- 2003 Fellow, AAAS
- 2004 Keynote Address: Tenth Intl. Toxicology Congress, Finland
- 2005 Keynote Address: Intl. Symposium, Chronic Oxidative Stress and Cancer, German Cancer Res. Ctr., Heidelberg
- 2005 Keynote Address and Visiting Prof.: Frontiers in Biomedical Research, Hong Kong Sch. of Med., Hong Kong
- 2006 Keynote Address: Microenvironment and Cancer Symposium, Tokyo
- 2006 Presidential Address: International Congress on Liver Cancer, Shanghai
- 2007 State of the Science Address, International Liver Cancer Association, Barcelona
- 2007 Outstanding Mentor Award, NCI
- 2007-10 Chairman, Board of Directors, Keystone Symposia on Molecular and Cellular Biology
- 2009 NIH Merit Award
- 2009 AACR-Princess Takamatsu Award, AACR Annual Meeting, Denver, CO

EDITORIAL

Editor-in-Chief, *Carcinogenesis*

SELECTED PUBLICATIONS (The following are selected from over 500; *, top ten; †, top five in last 5 years)

- * 1. Harris, C. C., Autrup H., Connor, R., Barrett, L., McDowell, E. and Trump, B.: Interindividual variation in binding of benzo[a]pyrene to DNA in cultured human bronchi. *Science*, 194: 1067-1069, 1976.
- 2. Nigro, J. M., Baker, S. J., Preisinger, A. C., Jessup, J. M., Hostetter, R., Cleary, K., Bigner, S. H., Davidson, N., Baylin, S., Devilee, P., Glover, T., Weston, A., Modali, R., Harris, C. C. and Vogelstein, B.: Mutations in the p53 gene occur in diverse human tumor types. *Nature* 342: 705-708, 1989.
- * 3. Hsu, I. C., Metcalf, R. A., Welsh, J., Sun, T., Wang, N. J. and Harris, C. C.: p53 gene mutational hotspot in human hepatocellular carcinomas from Qidong, China. *Nature* 350: 427-428, 1991.
- * 4. Hollstein, M., Sidransky, D., Vogelstein, B. and Harris, C. C.: p53 mutations in human cancers. *Science*, 253: 49-53, 1991.
- 5. Harris, C. C. and Hollstein, M. C.: Clinical implications of the p53 tumor suppressor gene. *New Engl. J. Med.* 329: 1318-1327, 1993.
- 6. Wang, X. W., Forrester, K., Yeh, H., Feitelson, M. A., Gu, J. and Harris, C. C.: Hepatitis B virus X protein inhibits p53 sequence-specific DNA binding, transcriptional activity, and association with transcription factor ERCC3. *Proc. Natl. Acad. Sci. USA*, 91: 2230-2234, 1994.
- * 7. Wang, X. W., Yeh, H., Schaeffer, L., Roy, R., Moncollin, V., Egly, J. M., Wang, Z., Friedberg, E. C., Evans, M. K., Taffe, B. G., Bohr, V. A., Weeda, G., Hoeijmakers, J. H. J., Forrester, K. and Harris, C. C.: p53 Modulation of TFIIH-associated nucleotide excision repair activity. *Nature Genet.*, 10: 188-195, 1995.
- 8. Forrester, K., Ambts, S., Lupold, S. E., Kapust, R. B., Weinberg, W. C., Felley-Bosco, E., Wang, X. W., Geller, D. A., Billiar, T. R. and Harris, C. C.: Nitric oxide-induced p53 accumulation and regulation of inducible nitric oxide

- synthase (NOS2) expression by wild-type p53. *Proc. Natl. Acad. Sci. USA*, 93: 2442-2447, 1996.
9. Wang, X. W., Vermeulen, W., Coursen, J. D., Gibson, M., Lupold, S. E., Forrester, K., Xu, G., Elmore, L., Yeh, H., Hoeijmakers, J. H. J., and Harris, C. C.: The XPB and XPD DNA helicases are components of the p53-mediated apoptosis pathway. *Genes and Development*, 10: 1219-1232, 1996.
 10. Ambs, S., Ogunfusika, M. O., Merriam, W. G., Bennett, W. P., Billiar, T. R. and Harris, C. C.: Upregulation of NOS2 expression in cancer-prone p53 knockout mice. *Proc. Natl. Acad. Sci. USA*, 95: 8823-8828, 1998.
 11. Hussain, S. P. and Harris, C. C.: Molecular epidemiology of human cancer: contribution of mutation spectra studies of tumor suppressor genes. *Cancer Res.*, 58: 4023-4037, 1998.
 - *12. Ambs, S., Merriam, W. G., Ogunfusika, M. O., Bennett, W. P., Ishibe, N., Hussain, S. P., Tzeng, E. E., Geller, D. A., Billiar, T. R. and Harris, C. C.: p53 and vascular endothelial growth factor regulate tumor growth of NOS2-Expressing human carcinoma cells. *Nature Med.*, 4: 1371-1376, 1998.
 13. Spillare, E. A., Robles, A. I., Wang, X. W., Shen, J. C., Yu, C. E., Schellenberg, G. D. and Harris, C. C.: p53-mediated apoptosis is attenuated in Werner syndrome cells. *Genes and Development* 13: 1355-1360, 1999.
 14. Hussain, S. P., Raja, K., Amstad, P. A., Sawyer, M., Trudel, L. J., Wogan, G. N., Hofseth, L. J., Shields, P. G., Billiar, T. R., Trautwein, C., Hohler, T., Galle, P. R., Phillips, D. H., Markin, R., Marrogi, A. J. and Harris, C. C.: Increased p53 mutation load in nontumorous human liver of Wilson disease and hemochromatosis: oxylradical overload diseases. *Proc. Natl. Acad. Sci. USA*, 97: 12770-12775, 2000.
 15. Wang, X. W., Tseng, A., Ellis, N. A., Spillare, E. A., Linke, S. P., Robles, A. I., Seker, H., Yang, Q., Hu, P., Beresten, S., Garfield, S. and Harris, C. C.: Functional interaction of p53 and BLM DNA helicase in apoptosis. *J. Biol. Chem.*, 276: 32948-32955, 2001.
 16. Nagashima, M., Shiseki, M., Miura, K., Hagiwara, K., Linke, S. P., Peduex, R., Wang, X. W., Riabowol, K. and Harris, C. C.: DNA damage-inducible gene p33ING2 negatively regulates cell proliferation through acetylation of p53. *Proc. Natl. Acad. Sci. USA*, 98: 9671-9676, 2001.
 - *17. Hofseth, L. J., Saito, S., Hussain, S. P., Espey, M. G., Miranda, K. M., Araki, Y., Jhappan, C., Higashimoto, Y., He, P., Linke, S. P., Zurer, I., Rotter, V., Wink, D. A., Appella, E., and Harris, C. C.: Nitric oxide-induced cellular stress and p53 activation in chronic inflammation. *Proc. Natl. Acad. Sci. USA*, 100: 143-148, 2003.
 18. Hofseth, L. J., Khan, M. A., Ambrose, M., Nikolayeva, O., Xu-Welliver, M., Kartalou, M., Hussain, S. P., Roth, R. B., Zhou, X., Mechanic, L. E., Zurer, I., Rotter, V., Samson, L. D. and Harris, C. C.: The adaptive imbalance in base excision repair enzymes generates microsatellite instability in chronic inflammation. *J. Clin. Invest.*, 112: 1887-1894, 2003.
 19. Sengupta, S., Linke, S. P., Peduex, R., Yang, Q., Farnsworth, J., Garfield, S. H., Valerie, K., Shay, J. W., Ellis, N. A., Wasylyk, B. and Harris, C. C.: BLM helicase-dependent transport of p53 to sites of stalled DNA replication forks modulates homologous recombination. *E.M.B.O. J.* 22: 1210-1222, 2003.
 20. Hussain, S. P., Trivers, G. E., Hofseth, L. J., He, P., Shaikh, I., Mechanic, L., Doja, S., Jiang, W., Subleski, J., Shorts, L., Haines, D., Laubach, V. E., Wiltrout,

- R. H., Djurickovic and Harris, C. C.: Nitric oxide, a mediator of inflammation, suppresses tumorigenesis. *Cancer Res.*, 64: 6849-6853, 2004.
21. Sengupta, S., Robles, A. I., Linke, S. P., Sinogeeva, N. I., Zhang, R., Pedoux, R., Ward, I. M., Celeste, A., Nussenzweig, A., Chen, J., Halazonetis, T. D. and Harris, C. C.: Functional interaction between BLM helicase and 53BP1 in a Chk1-mediated checkpoint pathway during S-phase arrest. *J. Cell Biol.*, 166: 801-813, 2004.
 22. Staib, F., Robles, A. I., Varticovski, L., Wang, X. W., Zeeberg, B. R., Sirotin, M., Zhurkin, V. B., Hofseth, L. J., Hussain, S. P., Weinstein, J. N., Galle, P. R. and Harris, C. C.: The p53 tumor suppressor network is a key responder to microenvironmental components of chronic inflammation stress. *Cancer Res.* 65: 10255-10264, 2005.
 23. Yang, Q., Zheng, Y.-L. and Harris, C. C.: POT1 and TRF2 cooperate to maintain telomeric integrity. *Mol. Cell. Biol.*, 25: 1070-1080, 2005.
 24. Volinia, S., Calin, G. A., Liu, C. G., Ambs, S., Cimmino, A., Petrocca, F., Visone, R., Iorio, M., Roldo, C., Ferracin, M., Prueitt, R. L., Yanaihara, N., Lanza, G., Scarpa, A., Vecchione, A., Negrini, M., Harris, C. C. and Croce, C. M.: A microRNA expression signature of human solid tumors defines cancer gene targets. *Proc. Natl. Acad. Sci. USA* , 103: 1-5, 2006.
 25. Unoki, M., Shen, J. C., Zheng, Z. M. and Harris, C. C.: Novel splice variants of ING4 and their possible roles in the regulation of cell growth and motility. *J. Biol. Chem.*, 281: 34677-34686, 2006.
 - *†26. Yanaihara, N., Caplen, N., Bowman, E., Kumamoto, K., Yi, M., Stephens, R. M., Okamoto, A., Yokota, A., Tanaka, T., Calin, G. A., Liu, C. G., Croce, C. M. and Harris, C. C.: microRNA expression signature predicts lung cancer diagnosis and prognosis. *Cancer Cell* 9: 189-198, 2006.
 - *†27. Seike, M., Yanaihara, N., Bowman, E. D., Zanetti, K. A., Budhu, A., Kumamoto, K., Mechanic, L. E., Matsumoto, S., Yokota, J., Shibata, T., Sugimura, H., Gemma, A., Kudoh, S., Wang, X. W., and Harris, C. C.: Use of a cytokine gene expression signature in lung adenocarcinoma and the surrounding tissue as a prognostic classifier. *J. N. C. I.*, 99: 1257-1269, 2007.
 - *28. Pine, S. R., Mechanic, L. E., Ambs, S., Bowman, E. D., Chanock, S. J., Loffredo, C., Shields, P. G., and Harris, C. C.: Lung cancer survival and functional polymorphisms in MBL2, an innate-immunity gene. *J. N. C. I.*, 99: 1401-1409, 2007.
 29. Yoshikawa, H., Matsubara, K., Zhou, X., Okamura, S., Kubo, T., Murase, Y., Shikauchi, Y., Esteller, M., Herman, J. G., Wang, X. W. and Harris, C. C.: WNT10B functional dualism: beta-catenin/Tcf-dependent growth promotion or independent suppression with deregulated expression in cancer. *Molec. Biol. Cell*, 18: 4292-4303, 2007.
 30. Yang, Q., Horikawa, I., Zhang, R., Afshar, Y., Kokko, A., Laiho, P., Aaltonen, L. A., and Harris, C. C.: Functional diversity of human POT1 isoforms in telomere protection and cellular senescence. *Cancer Res.*, 67:11677-11686, 2007.
 - *†31. Schetter, A. J., Leung, S. Y., Sohn, J. J., Zanetti, K. A., Bowman, E. D., Yanaihara, N., Yuen, S. T., Chan, T. L., Kwong, D.L.W., Au, G. K. H., Liu, C. G., Calin, G. A., Croce, C. M., and Harris, C. C.: MicroRNA expression profiles associated with prognosis and therapeutic outcome in colon adenocarcinoma. *JAMA*, 299: 425-436, 2008.
 32. Seike, M., Goto, A., Okano, T., Bowman, E. D., Schetter, A. J., Horikawa, I., Mathe, E. A., Jen, J., Yang, P., Sugimura, H., Gemma, A., Kudoh, S., Croce, C.

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33. Fujita, F., Mondal, A. M., Horikawa, I., Nguyen, G. H., Kumamoto, K., Sohn, J. J., Bowman, E. D., Mathe, E. A., Schetter, A. J., Pine, S. R., Ji, H., Vojtesek, B., Bourdon, J. C., Lane, D. P., and Harris, C. C.: p53 isoforms $\Delta 133p53$ and p53 β are endogenous regulators of replicative cellular senescence. *Nat Cell Biology*, 11: 1135-1142, 2009.
34. Olivo-Marston, S. E., Yang, P., Mechanic, L. E., Bowman, E. D., Pine, S. R., Loffredo, C. A., Alberg, A. J., Caporaso, N., Shields, P. G., Chanock, S., Wu, Y., Jiang, R., Cunningham, J., Jen, J. and Harris, C. C.: Childhood exposure to secondhand smoke and functional mannose binding lectin polymorphisms are associated with increased lung cancer risk. *Cancer Epidemiol Biomarkers Prev.*, 18: 3375-3383, 2009.
- †35. Pine, S. R., Ryan, B. M., Varticovski, L., Robles, A. I. and Harris, C. C.: Microenvironmental modulation of asymmetric cell division in human lung cancer cells. *Proc Natl Acad Sci USA*, 107: 2195-2200, 2010.