


PERSONAL INFORMATION

Stephen Hecht

WORK EXPERIENCE

- 1996–Present  Wallin Land Grant Professor of Cancer Prevention and Professor Masonic Cancer Center, University of Minnesota, Minneapolis (United States)
Head, Carcinogenesis and Chemoprevention Program, 1998-2014
Member, Medicinal Chemistry and Pharmacology Graduate Programs, 1996-present

EDUCATION AND TRAINING

- 1964– Duke University, B.S. (with honors), Chemistry
1968– Massachusetts Institute of Technology, Ph.D., Organic Chemistry

ADDITIONAL INFORMATION

Expertise

Publications

Selected Contributions to Science (with key references)

1. Tobacco-specific nitrosamines: identification in tobacco products, carcinogenicity, and metabolism (early studies). Working at the American Health Foundation, founded by Ernst Wynder, Dietrich Hoffmann and I identified the carcinogen N'-nitrosornicotine (NNN) in unburned tobacco, with unusually high levels in certain products. This was the first identification of a carcinogen in unburned tobacco; it was previously assumed that tobacco carcinogens were formed only during combustion. This finding encouraged exploration of the chemistry of nicotine nitrosation, which resulted in the first identification of NNK, among other products. We tested NNK and found that it was a powerful lung carcinogen in rats and other laboratory animals. In a series of studies, my group and others at the Foundation elucidated most of the known metabolic and DNA binding pathways of NNN and NNK, leading ultimately to regulation proposals.
 - a. Hoffmann, D., Hecht, S.S., Ornaf, R.M., and Wynder, E.L. N'-nitrosornicotine in tobacco. *Science*, 186: 265-267, 1974.
 - b. Hecht, S.S., Chen, C.B., Ornaf, R.M., Jacobs, E., Adams, J.D., and Hoffmann, D. Reaction of nicotine and sodium nitrite: Formation of nitrosamines and fragmentation of the pyrrolidine ring. *J. Org. Chem.*, 43: 72-76, 1978.
 - c. Hecht, S.S. Biochemistry, biology, and carcinogenicity of tobacco-specific N-nitrosamines. *Chem. Res. Toxicol.*, 11: 559-603, 1998.
 - d. Hecht, S.S. It is time to regulate carcinogenic tobacco-specific nitrosamines in cigarette tobacco. *Cancer Prev. Res.*, 7: 639-647, 2014.
2. Development of the NNAL biomarker and application in studies of secondhand tobacco smoke exposure. We identified NNAL as a carcinogenic metabolite of NNK, formed in virtually all systems examined including humans. This led to the proposal that it could be a biomarker of lung carcinogen NNK uptake. The tobacco-specificity of NNK and NNAL were particularly attractive in this respect. We developed analytical methods to quantify NNAL and its glucuronides in human urine – these are now widely used to assess exposure to NNK; thousands of analyses have been published. The NNAL biomarker was particularly appropriate for investigation of secondhand tobacco smoke exposure because it linked this exposure to lung cancer; these studies helped to support the clean indoor air regulations which are now universal.
 - a. Carmella, S.G., Akerkar, S., and Hecht, S.S. Metabolites of the tobacco-specific nitrosamine 4 (methylnitrosamino)-1-(3-pyridyl)-1-butanone in smokers' urine. *Cancer Res.*, 53: 721-724, 1993.
 - b. Hecht, S.S., Carmella, S.G., Murphy, S.E., Akerkar, S., Brunnemann, K.D., and Hoffmann, D. A tobacco-specific lung carcinogen in the urine of men exposed to cigarette smoke. *New Engl. J. Med.*, 329: 1543-1546, 1993.
 - c. Anderson, K.E., Carmella, S.G., Ye, M., Bliss, R.L., Le, C., Murphy, L., and Hecht, S.S. Metabolites of a tobacco-specific lung carcinogen in nonsmoking women exposed to environmental tobacco

smoke. *J. Natl Cancer Inst.*, 93: 378-381, 2001.

d. Hecht, S.S., Stepanov, I., and Carmella, S.G. Exposure and metabolic activation biomarkers of carcinogenic tobacco-specific nitrosamines. *Accounts Chem. Res.* 49: 106-114, 2016.

3. Application of tobacco carcinogen and toxicant biomarkers in clinical and epidemiologic studies: relevance to cancer risk. A panel of tobacco carcinogen and toxicant biomarkers has been developed, using liquid chromatography-mass spectrometric techniques to analyze urine, blood, or DNA. These methods have been applied in multiple collaborative studies, mainly with Professors Dorothy Hatsukami and Jian-Min Yuan, to explore human exposure and risk. The recent CENIC trial of reduced nicotine cigarettes is one example. Using samples from nested case-control studies within prospective cohorts, NNAL, cotinine, and phenanthrene tetraol, and 8-epi-prostagalndin F2 α were significantly related to lung cancer; and NNN was significantly related to esophageal cancer, after correction for number of years of cigarette smoking and number of cigarettes per day. These results indicate that these biomarkers could become part of a predictive algorithm for cancer risk in smokers.

a. Hecht, S.S., Murphy, S.E., Carmella, S.G., Zimmerman, C.L., Losey, L., Kramarczuk, I., Roe, M.R., Puumala, S.S., Li, Y.S., Le, C., Jensen, J., and Hatsukami, D. Effects of reduced cigarette smoking on uptake of a tobacco-specific lung carcinogen. *J. Natl. Cancer Inst.*, 96: 107-115, 2004.

b. Hatsukami, D.K., Luo, X., Jensen, J.A., al'Absi, M., Allen, S.S., Carmella, S.G., Chen, M., Cinciripini, P.M., Denlinger-Apte, R., Drobles, D.J., Koopmeiners, J.S., Lane, T., Le, C.T., Leischow, S., Luo, K., McCleron, J., Murphy, S.E., Paiano, V., Robinson, J.D., Severson, H., Sipe, C., Strasser, A.A., Strayer, L.G., Tang, M.K., Vandrey, R., Hecht, S.S., Benowitz, N.L., and Donny, E.C., Effect of immediate vs. gradual reduction in nicotine content of cigarettes on biomarkers of smoke exposure: a randomized clinical trial, *J. Amer. Med. Assoc.*, 320: 880-891, 2018.

c. Yuan, J-M., Butler, L.M., and Hecht, S.S. Urinary tobacco constituent biomarkers for risk prediction of smoking-related lung cancer. *Cancer Res.* 74: 401-411, 2014. PMID: PMC4066207

d. Yuan, J-M., Carmella, S.G., Wang, R., Yan, Y., Adams-Haduch, J., Gao, Y-T, and Hecht, S.S. Relationship of the oxidative damage biomarker 8-epi-prostagalndin F2 α to risk of lung cancer development in the Shanghai Cohort Study. *Carcinogenesis*, 39: 948-954, 2018.

4. Metabolism and DNA adducts of polycyclic aromatic hydrocarbons (PAH) and aldehydes. We carried out extensive studies on metabolism and DNA adduct formation by PAH, important carcinogens in tobacco smoke. The results of these studies were consistent with, expanded, and supported the bay region diol epoxide model of PAH carcinogenicity, leading to development of the phenanthrene tetraol biomarker of PAH exposure plus metabolic activation. Our studies on nitrosamine metabolism led to investigations of related metabolically formed aldehydes, and the identification of DNA adducts of formaldehyde, acetaldehyde, acrolein and crotonaldehyde in human tissues. The acetaldehyde-DNA adducts are particularly relevant to alcohol consumption and its role in carcinogenesis.

a. Hecht, S.S., Amin, S., Huie, K., Melikian, A.A., and Harvey, R.G. Enhancing effect of a bay region methyl group on tumorigenicity in newborn mice and mouse skin of enantiomeric bay region diol epoxides formed stereoselectively from methylchrysenes in mouse epidermis. *Cancer Res.*, 47: 5310-5315, 1987.

b. Yang, J., Balbo, S., Villalta, P.W., and Hecht, S.S. Analysis of acrolein-derived 1,N2-propanoexyguanosine adducts in human lung DNA from smokers and non-smokers, *Chem. Res. Toxicol.*, 32: 318-325, 2019.

c. Wang, M., Cheng, G., Balbo, S., Carmella, S.G., Villalta, P.W., and Hecht, S.S. Clear differences in levels of a formaldehyde-DNA adduct in leukocytes of smokers and non-smokers. *Cancer Res.*, 69: 7170-7174, 2009. PMID: PMC2745488.

d. Balbo, S., Meng, L., Bliss, R.L., Jensen, J.A., Hatsukami, D.K., and Hecht, S.S. Kinetics of DNA adduct formation in the oral cavity after drinking alcohol. *Cancer Epidemiol. Biomarkers & Prev.* 21: 601-608, 2012. PMID: PMC3319307.

5. Expertise in tobacco carcinogenesis. Years of experience in this area have led to service on multiple national and international committees evaluating various aspects of the tobacco and cancer problem, along with the preparation of reviews and book chapters on aspects of tobacco carcinogenesis.

a. Hecht, S.S. Biochemistry, biology, and carcinogenicity of tobacco-specific N-nitrosamines. *Chem. Res. Toxicol.*, 11: 559-603, 1998.

b. Hecht, S. S. Tobacco smoke carcinogens and lung cancer. *J. Natl. Cancer Inst.*, 91: 1194-1210, 1999.

c. Hecht, S.S. Tobacco carcinogens, their biomarkers and tobacco-induced cancer. *Nature Rev. Cancer*, 3: 733-744, 2003.

d. Hecht, S.S. DNA damage by tobacco carcinogens. In: *Carcinogens, DNA Damage and Cancer*

Risk (M.C. Poirier, ed.), New Jersey: World Scientific, 2018, pp 69-85.

Link to Bibliography Over 850 publications including more than 590 peer-reviewed journal articles and over 250 book chapters and related publications; control plus click to follow link
<http://www.ncbi.nlm.nih.gov/sites/myncbi/stephen.hecht.1/bibliography/41146177/public/?sort=date&direction=ascending>

Projects

Memberships

American Association for Cancer Research
American Association for the Advancement of Science
American Chemical Society
American Society of Preventive Oncology
American Society for Mass Spectrometry
International Society for the Study of Xenobiotics
Society for Research on Nicotine and Tobacco
American Society for Pharmacology and Experimental Therapeutics

Other Relevant Information

Honors and Awards

Academy for Excellence in Team Science, University of Minnesota, 2019
Listed in AACR Landmarks in Cancer Research, 2017: Tobacco-Specific Nitrosamines, JNCI 60: 819-824 (1978)
University of Minnesota Medical School Dean's Distinguished Research Lectureship, 2017
American Chemical Society Minnesota Section, Minnesota Award, 2017
University of Minnesota Medical School Wall of Scholarship, 2015
Elected American Association for the Advancement of Science Fellow, 2014
Selected as next Editor-In-Chief, Chemical Research in Toxicology, American Chemical Society, 2012
Joseph Cullen Award, American Society of Preventive Oncology, 2012
Elected American Chemical Society Fellow, 2009
Founders' Award, Division of Chemical Toxicology, American Chemical Society, 2009
Academy for Excellence in Health Research, Academic Health Center, University of Minnesota, 2006
American Association for Cancer Research-Cancer Research and Prevention Foundation Award for Excellence in Cancer Prevention Research, 2006
Merit Award, National Cancer Institute, 2004-2014
Dr. William Cahan Distinguished Professor Award, Flight Attendant Medical Research Institute, 2002
Alton Ochsner Award Relating Smoking and Health, 2001
American Cancer Society Research Professor, 2000-2009
Wallin Chair in Cancer Prevention, Masonic Cancer Center, University of Minnesota, 1996-
Endowed Chair in Carcinogenesis and Chemoprevention, American Health Foundation, 1992-1996
Cancer Research Covers: March 1, 1988; February 15, 1993
Chemical Research in Toxicology Covers: June 1998, July 2007, February 2011
Cancer Epidemiology Biomarkers & Prevention Cover, December 2003
Outstanding Investigator Grant, National Cancer Institute, 1987-2001
Research Career Development Award, National Cancer Institute, 1975-1980
National Research Council Fellow, 1971-1973
Phi Beta Kappa, 1964
Current Research Interests
☰ Mechanisms and prevention of tobacco-induced cancer
☰ Carcinogen biomarkers and their application in molecular epidemiology and cancer prevention
☰ Mechanisms of chemical carcinogenesis in humans

☰ Chemoprevention of cancer