BIOGRAPHICAL SKETCH

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NAME: Zarbl, Helmut

eRA COMMONS USER NAME (credential, e.g., agency login): HZARBL

POSITION TITLE: Professor and Chair, Environmental and Occupational Health and Justice

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Marianopolis College, Montreal, Canada	D.C.S	1973-1975	Health Sciences
McGill University, Montreal, Canada	B.Sc	1975-1978	Biochemistry
McGill University, Montreal, Canada	Ph.D	1978-1983	Biochemistry
NIH - Frederick Cancer Research Facility, MD	Post-doc	1983-1985	Cancer Biology
Clinical Research Institute of Montreal, Canada	Post-doc	1985-1987	Cancer Genetics

A. Personal Statement

I have been continuously funded by NIH since beginning my career at MIT in 1987, an achievement that I attribute to the continuous availability state-of-the-art facility cores and pilot funding from two Cancer Centers and three NIEHS Core Centers (MIT, U. Washington, and Rutgers). Centers also provided me with my first experiences in community outreach and engagement and allowed me to develop a passion for community-based research. Even early in my career, Centers provided me opportunities to develop leadership and administrative skills essential for running transdiciplinary research programs, mentoring early career faculty, and developing new programs. My interdisciplinary research experience has also allowed me to lead the Fred Hutchinson Cancer Research Center/University of Washington (FHCRC/UW) Toxicogenomics Consortium, serve as the Associate Director for Public Health Sciences at the Cancer Institute of New Jersey, and eventually become the Director of the NIEHS P30 Center at Rutgers. My Centers experience has led to contributions to national policy by serving on research reviews, external advisory boards and committees, including the National Academy of Sciences' National Research Council Committee on the Applications of Toxicogenomics to Predictive Toxicology.

My research focuses on understanding the molecular, genetic and epigenetic mechanisms that contribute to toxicity, mutagenesis, carcinogenesis, genetic susceptibility, genomics and chemoprevention. As a postdoctoral fellow, I worked with Mariano Barbacid on role of oncogene mutations in carcinogenesis. My research using both animal and *in vitro* model systems increased our understanding the molecular mechanisms of chemical carcinogenesis. I then went to work as a postdoc in the laboratory of Paul Jolicoeur, where I developed a somatic cell approach to screening for tumor suppressor genes. I subsequently accepted a faculty position at MIT where I continued the analysis of oncogene activation, mechanisms of signal transduction, tumor suppressor inactivation. At MIT I was a Member of their Center for Environmental Health Sciences, and eventually became the Deputy Director. After 8 years at MIT, I joined the Fred Hutchinson Cancer Center (FHCRC) in Seattle, where we initiated genetic linkage studies using epigenetic markers, as well as studies on endocrine disruptors and circadian rhythm as an epigenetic regulator of carcinogenesis. In Seattle I also became a member of the University of Washington Center for Ecogenetics and Environmental Health (CEEH), serving as the Director of the Environmental Carcinogenesis and Genomics Cores. While at the FHCRC, I also initiated, designed, staffed, and directed the Center's highly successful DNA Microarray Facility, and helped the UW Center for Ecogenetics and Environmental Health design a satellite facility. I leveraged the genomics facility to successfully compete

for a NIEHS grant to develop and direct the Seattle Toxicogenomics Research Consortium, which was part of a national consortium comprising eight Centers around the US, serving as the Director of the National Consortium's steering committee for two years. In addition, I served as the founding Director of the FHCRC's successful Industrial Liaison Program, whose mission was to develop academic-industry partnerships. After moving to the University of Medicine and Dentistry of New Jersey (now Rutgers), I assumed the leadership of and twice renewed the Center for Environmental Exposures and Disease. I also helped the Rutgers Cancer Institute of New Jersey secure a five-year renewal by directing, reorganizing, and strengthening their Division of Public Health Sciences, as well as establishing a Functional Genomics Shared Resources. My research has remained on the cutting edge, discovering new cancer susceptibility genes that serve as new biomarkers for cancer diagnosis and prognosis, new epigenetic biomarkers of risk associated with disruption of circadian rhythm, and biomarkers of transgenerational effects of endocrine disruptors on sexual development, reproduction, and cancer risk. My most recent research focuses on the assessing the mutagenicity of nanoparticles in an innovative approach that combines organ-on-a-chip technology with duplex DNA sequencing, the highly sensitive assay that allows for the detection of low frequency mutations (10^{-8}) in exposed cells. I have also played a major role on National Academy panels and standing committees looking at emerging science for environmental health decisions, including the organization of workshops on the exposome, epigenetics, the microbiome, and big data, among others. In summary, I have significant experience in establishing, overseeing, and motivating researchers in large programs that coordinate cutting edge research cutting edge technologies within and across Centers.

Highlighted Ongoing Research Support

P30 Zarbl, (P) 04/01/1997 - 03/31/2024
Rutgers Center for Environmental Exposure and Disease (CEED)
Role: PI

P30 (Pilot Grant) Zarbl (PI) 04/01/22 – 03/31/23
Assessing the Toxicity and Mutagenicity of Micro- Nanoplasitics Using an In Vitro Small Intestinal Epithelium Model and Duodenum-on-a-Chip Technology
Role:PI

P30 (Pilot Grant) Demokritou (PI) 04/01/22 – 03/31/23
Development of a Human Intestine-on-Chip (IOC) Mechanistic Toxicity Testing Platform for Ingested Micro- and Nano-plastics (MNPs)
Role: co-PI

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2017-	Director, Environmental and Occupational Health Sciences Institute (EOHSI), Rutgers, Piscataway, NJ
2017-	Chair, Environmental and Occupational Health and Justice, Rutgers School of Public Health, Piscataway,NJ.
2008-2013	Associate Director, Division of Public Health Sciences, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2007-	Director, Rutgers NIEHS Center for Environmental Exposures and Disease.
2006-	Professor, Environmental and Occupational Medicine, Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Rutgers, Piscataway, NJ
2002-2004	Director, Industrial Liaison Program, FHCRC, Seattle, WA
2000-	Visiting Professor of Genetics, China Medical University, Shenyang, China
2000-2006	Director, NIEHS - FHCRC/UW Toxicogenomics Research Consortium, Seattle, WA
1998-2002	Director, Public Health Sciences Core Laboratory, FHCRC, Seattle, WA
1998-2002	Scientific Director, DNA Microarray Shared Resource, FHCRC, Seattle, WA
1996-2006	Affiliate Professor, Departments of Environmental and Occupational Health & Pathology, University of Washington, Seattle, WA
1995- 2006	Member, Center for Ecogenetics and Environmental Health, UW, Seattle, WA

1994-2006 Member, Divisions of Human Biology & Public Health Sciences, Fred Hutchinson Cancer Research Center (FHCRC), Seattle, WA
1992-1994 Associate Professor, Division of Toxicology, Whitaker College of Health Sciences and Technology Massachusetts Institute of Technology, Cambridge, MA
1987-1992 Assistant Professor, Department Applied Biological Sciences, Massachusetts Institute of Technology, Cambridge, MA

Other Experience and Professional Memberships

2010-2014 Vice President (elect), VP, President, and Past President Carcinogenesis Specialty Section, Society for Toxicology
2009-Member, National Academy of Sciences, National Research Council Standing Committee on "Emerging Science for Environmental Health Decisions"
2009 NIEHS Superfund Basic Research Program, External Advisory Panel
2009-2015 External Scientific Advisory Board Superfund Basic Research Program University of North Carolina. Chapel Hill, NC
2008-2010 Chair, Disease Prevention Task Force, Society of Toxicology
2008 EPA-IRIS Peer Review Panel: Toxicological Review of 1,2,3-Trichlropropane
2006- 2008 Editor-In Chief, Biological Procedures Online
2002–2004 Associate Editor, Environmental Health Perspectives: Toxicogenomics
2000–2002 Associate Editor, Cancer Research (AACR)
1999 Chair, External Scientific Advisory Board Member, Research Center for Minority Institutions, Clark Atlanta University, Atlanta, GA
1993-1994 Associate Director, M.I.T. Center for Environmental Health Sciences

Honors

2012 Women in Toxicology Mentoring Award from the Society of Toxicology
2008- Fellow of the Academy of Toxicological Sciences
1988-1989 Robert A. Swanson Assistant Professor in Life Sciences

C. Contributions to Science

1. My early research was among the first to demonstrate that mutagenic chemicals also induce genetic and epigenetic changes in oncogenes in vitro and in vivo that these changes contribute to carcinogenesis.

   a. Zarbl H, Sukumar S, Arthur AV, Martin-Zanca D, Barbacid M. Direct mutagenesis of Ha-ras-1 oncogenes by N-nitroso-N-methylurea during initiation of mammary carcinogenesis in rats. Nature. 1985;315(6018):382-5. PMID: 3923365
   b. Cha RS, Thilly WG, Zarbl H. N-nitroso-N-methylurea-induced rat mammary tumors arise from cells with preexisting oncogenic Hras1 gene mutations. Proceedings of the National Academy of Sciences of the United States of America. 1994;91(9):3749-53. PMCID: PMC43659
   c. Jin Z, Houle B, Mikheev AM, Cha RS, Zarbl H. Alterations in H-ras1 promoter conformation during N-nitroso-N-methylurea-induced mammary carcinogenesis and pregnancy. Cancer research. 1996;56(21):4927-35. PMID: 8895746
   d. Mikheev AM, Inoue A, Jing L, Mikheeva SA, Li V, Leanderson T, Zarbl H. Frequent activation of CArG binding factor-A expression and binding in N-methyl-N-nitrosourea-induced rat mammary carcinomas. Breast cancer research and treatment. 2004;88(1):95-102. PMID: 15538050

2. My subsequent research focused on the development and use of *in vitro* assays and genetic linkage analysis to identify tumor suppressor /susceptibility genes that confer susceptibility to mammary carcinogenesis. These studies led to the identification of the FRY mammary carcinogenesis susceptibility gene which is being developed as novel tool for cancer diagnostics and prognosis.

   a. Zarbl H, Latreille J, Jolicoeur P. Revertants of v-fos-transformed fibroblasts have mutations in cellular genes essential for transformation by other oncogenes. Cell. 1987;51(3):357-69. PMID: 3664639
   b. Athanassiou M, Hu Y, Jing L, Houle B, Zarbl H, Mikheev AM. Stabilization and reactivation of the p53 tumor suppressor protein in nontumorigenic revertants of HeLa cervical cancer cells. Cell growth &

differentiation : the molecular biology journal of the American Association for Cancer Research. 1999;10(11):729-37. PMID: 10593649

c. Mikheev AM, Mikheeva SA, Liu B, Cohen P, Zarbl H. A functional genomics approach for the identification of putative tumor suppressor genes: Dickkopf-1 as suppressor of HeLa cell transformation. Carcinogenesis. 2004;25(1):47-59. PMID: 14555616

d. Ren X, Graham JC, Jing L, Mikheev AM, Gao Y, Lew JP, Xie H, Kim AS, Shang X, Friedman C, Vail G, Fang MZ, Bromberg Y, Zarbl H. Mapping of Mcs30, a new mammary carcinoma susceptibility quantitative trait locus (QTL30) on rat chromosome 12: identification of fry as a candidate Mcs gene. PloS one. 2013;8(9):e70930. PMCID: PMC3759375

3. My laboratory was also among the first to use genomics to study mechanisms of toxicity and carcinogenicity. In 1997, I initiated, designed, staffed, and directed the microarray facility at the Fred Hutchinson Cancer Research Center (FHCRC). As a result, I was able to organize and direct the NIEHS sponsored FHCRC/University of Washington Toxicogenomics Consortium and served as the Chair of the Steering Committee for the NIEHS National Toxicogenomics Consortium for two years. Our findings helped establish standards in the field and performed mechanistic studies of toxicant exposures.

   a. Bammler T, Beyer RP, Bhattacharya S, Boorman GA, Boyles A, Bradford BU, Bumgarner RE, Bushel PR, Chaturvedi K, Choi D, Cunningham ML, Deng S, Dressman HK, Fannin RD, Farin FM, Freedman JH, Fry RC, Harper A, Humble MC, Hurban P, Kavanagh TJ, Kaufmann WK, Kerr KF, Jing L, Lapidus JA, Lasarev MR, Li J, Li YJ, Lobenhofer EK, Lu X, Malek RL, Milton S, Nagalla SR, O'Malley J P, Palmer VS, Pattee P, Paules RS, Perou CM, Phillips K, Qin LX, Qiu Y, Quigley SD, Rodland M, Rusyn I, Samson LD, Schwartz DA, Shi Y, Shin JL, Sieber SO, Slifer S, Speer MC, Spencer PS, Sproles DI, Swenberg JA, Suk WA, Sullivan RC, Tian R, Tennant RW, Todd SA, Tucker CJ, Van Houten B, Weis BK, Xuan S, Zarbl H, Members of the Toxicogenomics Research C. Standardizing global gene expression analysis between laboratories and across platforms. Nature methods. 2005;2(5):351-6. PMID: 15846362 (Presented on the Cover)

   b. Beyer RP, Fry RC, Lasarev MR, McConnachie LA, Meira LB, Palmer VS, Powell CL, Ross PK, Bammler TK, Bradford BU, Cranson AB, Cunningham ML, Fannin RD, Higgins GM, Hurban P, Kayton RJ, Kerr KF, Kosyk O, Lobenhofer EK, Sieber SO, Vliet PA, Weis BK, Wolfinger R, Woods CG, Freedman JH, Linney E, Kaufmann WK, Kavanagh TJ, Paules RS, Rusyn I, Samson LD, Spencer PS, Suk W, Tennant RJ, Zarbl H, Members of the Toxicogenomics Research C. Multicenter study of acetaminophen hepatotoxicity reveals the importance of biological endpoints in genomic analyses. Toxicological sciences : an official journal of the Society of Toxicology. 2007;99(1):326-37. PMID: 17562736

   c. Ricicki EM, Luo W, Fan W, Zhao LP, Zarbl H, Vouros P. Quantification of N-(deoxyguanosin-8-yl)-4-aminobiphenyl adducts in human lymphoblastoid TK6 cells dosed with N-hydroxy-4-acetylaminobiphenyl and their relationship to mutation, toxicity, and gene expression profiling. Analytical chemistry. 2006;78(18):6422-32. PMID: 16970317

   d. Ren X, Zhang X, Kim AS, Mikheev AM, Fang M, Sullivan RC, Bumgarner RE, Zarbl H. Comparative genomics of susceptibility to mammary carcinogenesis among inbred rat strains: role of reduced prolactin signaling in resistance of the Copenhagen strain. Carcinogenesis. 2008;29(1):177-85. PMID: 17916903

4. I first became interested in the role of zeranol in mammary carcinogenesis and development and in 2004 responded to an RFA from NIEHS targeting endocrine disruptors (ED). Although the grant (1R21ES013860-01) was not funded, my dedication and determination to study this potentially import human ED was undaunted. In 2007, I was awarded a grant from the New Jersey Cancer Commission (09-1077-CCR-EO) to study the transgenerational effects of dietary zeranol and sexual development and breast cancer. This study led to population-based study of zeranol and puberty in prepubescent girls, and allowed us to perform a three-generation study of in utero zeranol exposure in rats at doses permitted in the human diet by the FDA. This research set the stage for CEED's current multidisciplinary research program on mycoestrogens.

   a. Bandera EVC, U.; Buckley, B.; Lin, Y.; Isukapalli, S.; Marshall, I.; King, M.; Zarbl, H. Urinary mycoestrogens, body size and breast development in New Jersey girls. The Science of the total environment. 2011;409(24):5221-7. Epub 2011/10/07. PMCID: PMC3312601

b. Mukherjee D, Royce SG, Alexander JA, Buckley B, Isukapalli SS, Bandera EV, Zarbl H, Georgopoulos PG. Physiologically-based toxicokinetic modeling of zearalenone and its metabolites: application to the Jersey girl study. PloS one. 2014;9(12):e113632. PMCID: PMC4256163
c. Lewis, CA, Gallo, MA, Reuhl, K, Zarbl, H. In utero Exposure of Fisher 344 Rats to Low Doses of Zeranol via the Maternal Diet Produces Dose-Dependent Effects on Sexual Development and Reproduction. International Proceedings of Nutrition and Food Sciences 86:62-68 DOI: 10.7763/IPCBEE. 2015. V86. 10.

5. Our toxicogenomics studies also led us to discover that Methylseleocysteine (MSC), which is a potent chemopreventive agent, mediates its effects by restoring circadian rhythm disrupted in mammary cells by carcinogen. Our studies were the first to provide a mechanistic link between chemoprevention and circadian rhythm and elucidated the epigenetic mechanisms by which a chemopreventive regimen of MSC restores circadian gene expression. These studies showed that DNA damage response and repair genes are regulated by circadian rhythm, suggesting the proposed link between loss of circadian control of DNA repair, chronic diseases and aging. We further showed that MSC mediates its epigenetic effects by restoring regulation of Sirtuin 1 protein deacetylase activity. More recent studies indicate the disruption of circadian rhythm ablated normal responses of DNA damage response and repair genes the toxicants and stressors. Since shift work and exposure to light at night, which also disrupt circadian rhythm, have been classified as probable human mammary carcinogens by IARC, we also initiated an MSC intervention trial to determine if MSC could also restore peripheral cell rhythm is shift workers. Zhang, X and Zarbl, H. Chemopreventive Doses of Methylselenocysteine Alter Circadian Rhythm in Rat Mammary Tissue but Not Liver. Cancer Prevention Research 2(1):119-127, 2008.
   a. Ming Zhu Fang, Xun Zhang and Helmut Zarbl. (2010). Methylselenocysteine Inhibits Carcinogenesis by Enhancing Circadian Expression of Melatonin Receptor 1α and Estrogen Receptor β in Rat Mammary Epithelial Cells. Cancer Prevention Research 3(5): 640-652, 2010. PMCID: PMC2865563
   b. Fang MZ, Ohman-Strickland P, Kelly-McNeil K, Kipen H, Crabtree BF, Lew JP, Zarbl H. Sleep interruption associated with house staff work schedules alters circadian gene expression. Sleep medicine. 2015;16(11):1388-94. Epub 2015/10/27. PMCID: 4621493.
   c. Fang MZ, Guo WR, Kang H-G, Zarbl H. Enhancement of NAD+-dependent SIRT1 Deacetylase Activity by Methylselenocysteine Resets Circadian Clock in Carcinogen-Treated Mammary Epithelial Cells. Oncotarget 6(40): 42879-91. PMCID: PMC4767478
   d. Mingzhu Fang, Hwan-Goo Kang, Pamela Ohman-Strickland and Helmut Zarbl. (2017) Uncoupling Genotoxic Stress Responses from Circadian Control Increases Susceptibility to Mammary Carcinogenesis. Oncotarget 8(20):32752-32768. PMCID: PMC5464825

Complete List of Published Work in MyBibliography:
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