

## BIOGRAPHICAL SKETCH

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NAME Willett, Kristine L.	POSITION TITLE Associate Professor of Pharmacology		
eRA COMMONS USER NAME kwillett2005			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of North Carolina	B.A.	1993	Chemistry
Texas A&M University	Ph.D.	1997	Toxicology
Indiana University	Postdoc.	1997-98	Environ. Chemistry
Duke University	Postdoc.	1998-00	Toxicology

### A. Positions and Honors.

#### Positions and Employment

- 1990 Professional Intern, Oak Ridge National Laboratory, Environmental Sciences Division, Biogeochemistry Section.
- 1991 Summer Intern, Chemical Industries Institute of Toxicology, Experimental Pathology and Toxicology Division, Teratology Section.
- 1992 Summer Intern, Chemical Industries Institute of Toxicology, Experimental Pathology and Toxicology Division, Biochemical Toxicology Section.
- 1993 Research Assistant, Geochemical and Environmental Research Group, Texas A&M University, Department of Geosciences.
- 1997-98 Dreyfus Postdoctoral Fellow in Environmental Chemistry, Indiana University
- 1998-00 RJR Leon Golberg Fellowship in Toxicology, Duke University
- 2000-06 Assistant Professor of Pharmacology, Environmental Toxicology Research Program, University of Mississippi
- 2006- Associate Professor of Pharmacology, Environmental Toxicology Research Program, University of Mississippi

#### Professional Societies

Society of Toxicology (Molecular Biology Specialty Section); Society of Environmental Toxicology and Chemistry; American Association of Colleges of Pharmacy; Alpha Chi Sigma, Rho Chi.

### B. Selected peer-reviewed publications (in chronological order).

- 1) Willett, K.L., S.C. Loerch, and L.B. Willett. 1989. Effects of halogenated hydrocarbons on rumen microorganisms. *J. Veterinary Diagnostic Investigations*. 1:120-123.
- 2) Willett, K.L., R.R. Turner, and J.J. Beauchamp. 1992. Effect of chemical form of mercury on the performance of dosed soils in standard leaching protocols: EP and TCLP. *Hazardous Waste and Hazardous Materials*. 9:275-288.
- 3) Fister, T.F., G.S. Strossman, K.L. Willett, R.W. Odom, and R.W. Linton. 1995. In situ analysis of organic monolayers and their reactivity on single micrometer-sized particles by time-of-flight secondary ion mass spectrometry. *International J. of Mass Spectrometry & Ion Processes*. 143:87-111.
- 4) Willett, K., M. Steinberg, J. Thomsen, T.R. Narasimhan, S. Safe, S. McDonald, K. Beatty, and M.C. Kennicutt. 1995. Exposure of killifish to benzo[a]pyrene: Comparative metabolism, DNA adduct formation and aryl hydrocarbon (Ah) receptor agonist activities. *Comparative Biochemistry and Physiology*. 112B:93-103.

- 4) Bowes, R.C., A.R. Parrish, M.A. Steinberg, K.L. Willett, W. Zhao, U. Savas, C.R. Jefcoat, S.H. Safe, and K.S. Ramos. 1996. Atypical cytochrome P-450 induction profiles in glomerular mesangial cells at the mRNA and enzyme level. *Biochemical Pharmacology*. 52:587-595.
- 5) McDonald, S., K. Willett, J. Thomsen, T.R. Narasimhan, K. Connor, K. Beatty, C. Erickson, and S. Safe. 1996. Sublethal detoxification responses to contaminant exposure associated with offshore production platforms. *Canadian J. Fisheries Aquatic Sciences*. 53:2606-2617.
- 6) Hoivik, D., C. Wilson, W. Wang, K. Willett, R. Barhoumi, R. Burghardt, and S. Safe. 1997. Studies on the relationship between estrogen receptor content, glutathione S-transferase  $\pi$  expression and induction by 2,3,7,8-tetrachlorodibenzo-p-dioxin and drug resistance in human breast cancer cells. *Archives of Biochemistry and Biophysics*. 348:174-182.
- 7) Fiedler, H., K. Cooper, S. Bergek, M. Hjelt, C. Rappe, M. Bonner, F. Howell, K. Willett, and S. Safe. 1998. PCDD, PCDF, and PCB in farm-raised catfish from Southeast United States. *Chemosphere*. 37:1645-1656.
- 8) Hoivik, D., K. Willett, C. Wilson, and S. Safe. 1997. Estrogen does not modulate 2,3,7,8-tetrachlorodibenzo-p-dioxin mediated effects in MCF-7 and Hepa 1c1c7 cells. *J. Biological Chemistry*. 272:30270-30274.
- 9) Willett, K.L., P. Gardinali, J. Sericano, T. Wade, and S.H. Safe. 1997. Characterization of the H4IIE rat hepatoma cell bioassay for the evaluation of environmental samples containing polynuclear aromatic hydrocarbons (PAHs). *Archives Environmental Contamination & Toxicology*. 32:442-448.
- 10) Willett, K.L., S.J. McDonald, M.A. Steinberg, K.B. Beatty, M. C. Kennicutt, and S. H. Safe. 1997. Biomarker sensitivity for polynuclear aromatic hydrocarbon contamination in two marine fish species collected in Galveston Bay, Texas. *Environmental Toxicology & Chemistry*. 16:1472-1479.
- 11) Willett, K.L., K. Randerath, G-D. Zhou, and S.H. Safe. 1998. Inhibition of CYP1A1 activities by the PAH fluoranthene. *Biochemical Pharmacology*. 55:831-839.
- 12) Willett, K.L., E.M. Ulrich, and R.A. Hites. 1998. Differential toxicity and environmental fates of hexachlorocyclohexane isomers. *Environmental Science and Technology*. 32:2197-2207.
- 13) Willett, K.L., C. Wilson, J. Thomsen, and W. Porter. 1999. Evidence for and against the presence of polynuclear aromatic hydrocarbon and 2,3,7,8-tetrachloro-p-dioxin binding proteins in marine mussels. *Aquatic Toxicology*. 48:51-64.
- 14) Willett, K.L., and R.A. Hites. 2000. Chemical actinometry: Using o-nitrobenzaldehyde to measure lamp intensity in photochemical experiments. *Journal of Chemical Education*. 77:900-902.
- 15) Willett, K.L., P.R. Gardinali, L.A. Lienesch, and R.T. Di Giulio. 2000. Comparative metabolism and excretion of benzo(a)pyrene in two species of Ictalurid catfish. *Toxicological Sciences*. 58:68-76.
- 16) Ulrich, E.M., K.L. Willett, A. Caperell-Grant, R.M. Bigsby, and R.A. Hites. 2001. Understanding enantioselective processes: A laboratory rat model for  $\alpha$ -hexachlorocyclohexane ( $\alpha$ -HCH) accumulation. *Environmental Science and Technology*. 35:1604-1609.
- 17) Willett, K.L., L.A. Lienesch, and R.T. Di Giulio. 2001. No detectable DNA excision repair in UV-exposed hepatocytes from two species catfish. *Comparative Biochemistry and Physiology*. 128C:349-358.
- 18) Willett, K.L., D. Wassenberg, L.A. Lienesch, W. Reichert, and R.T. Di Giulio. 2001. *In vivo* and *in vitro* inhibition of CYP1A-dependent activity in *Fundulus heteroclitus* by the polynuclear aromatic hydrocarbon (PAH) fluoranthene. *Toxicology and Applied Pharmacology*. 177:264-271.
- 19) Marsh, K.E., Willett, K.L., Foran, C.M. and Brooks, B.W. 2003. Aquatic Resources and Human Health. Chapter 3. *In "A Web of Connections: Achieving Sustainable Freshwater Systems."* Island Press. Eds: Holland, M.M., Blood, E. and Shaffer, L.R. pp 65-83.
- 20) Zhang, L., Khan, I.A., Willett, K.L., Foran, C.M. 2003. *In Vivo* effects of black cohosh and genistein on estrogenic activity and lipid peroxidation in Japanese medaka (*Oryzias latipes*). *Journal of Herbal Pharmacotherapy*. 3(3):33-50.
- 21) Contractor, R., Foran, C.M., Li, S., and Willett, K.L. 2004. Evidence of sex and tissue specific promoter methylation and the potential for ethinylestradiol-induced changes in Japanese medaka (*Oryzias latipes*) estrogen receptor and aromatase genes. *Journal of Toxicology and Environmental Health* 67A:1-22.
- 22) Annavarapu, S., Foran, C.M., Gardinali, P., Metzger, C., and Willett, K.L. 2004. Comparison of two sites in Mobile Bay using *in vivo* biomarkers in largemouth bass, sediment bioassays, and sediment contaminant analysis. *Archives of Environmental Contamination and Toxicology*. 46:502-510.

- 23) Butala, H., Metzger, C., Rimoldi, J., and Willett, K.L., 2004. Microsomal estrogen metabolism in channel catfish. *Marine Environmental Research*. 58:489-494.
- 24) Willett, K.L. and Bouldin, A.S., 2004. Development and assessment of an online elective toxicology course. *American Journal of Pharmaceutical Education*. 68 (#57):1-9.
- 25) Willett, K.L., Roth, R.A., and Walker, L. 2004. Workshop overview: Hepatotoxicity assessment for botanical dietary supplements. *Toxicological Sciences*. 79:4-9.
- 26) Tabanca, N., Khan, S.I., Bedir, E., Annavarapu, S., Willett, K.L., Khan, I.A., Kirimer, N., and Baser, K.H.C. 2004. Estrogenic activity of isolated compounds and essential oils of *Pimpinella* species from Turkey, Evaluated using a recombinant yeast screen. *Planta Medica*. 70:728-735.
- 27) Chaudhary, A.M. and Willett, K.L. 2006. Inhibition of human cytochrome CYP1 enzymes by flavonoids of St. John's wort. *Toxicology*. 217:194-205.
- 28) Zhu, N., Lightsey, D., Foroozesh, M., Alworth, W., Chaudhary, A., Willett, K.L., and Klein Stevens, C.L. 2006. Naphthoflavone propargyl ether inhibitors of cytochrome P450. *Journal of Chemical Crystallography*. 36:289-296.
- 29) Rao, K.V., Donia, M.S., Peng, J., Garcia-Palomero, E, Alonso, D., Martinez, A., Medina, M., Franzblau, S.G., Tekwani, B.L., Khan, S.I., Wahyuono, S., Willett, K.L., Hamann, M.T. 2006. Manzamine B and E and ircinal A related alkaloids from an Indonesian *Acanthostrongylophora* sponge and their activity against infectious, tropical parasitic and Alzheimer's diseases. *Journal of Natural Products*. 69:1034-1040.
- 30) Patel, M.R., Scheffler, B.E., and Willett, K.L. 2006. Effects of benzo(a)pyrene exposure on killifish (*Fundulus heteroclitus*) aromatase activities and mRNA. *Aquatic Toxicology*. 77:267-278.
- 31) Willett, K.L., Ganesan, S., Patel, M., Metzger, C., Quiniou, S., Waldbieser, G., Scheffler, B. 2006. In vivo and in vitro CYP1B mRNA expression in channel catfish. *Marine Environmental Research*. 62:S332-S336.
- 32) Wang, L., Scheffler, B.E. and Willett, K.L. 2006. CYP1C1 messenger RNA expression is inducible by benzo(a)pyrene in *Fundulus heteroclitus* embryos and adults. *Toxicological Sciences*. 93:331-340.
- 33) Chaudhary, A., Pechan, T., and Willett, K.L. 2007. Differential protein expression of peroxiredoxin I and II by benzo(a)pyrene and quercetin treatment in 22 Rv1 and PrEC prostate cell lines. *Toxicology and Applied Pharmacology*. 220:197-210.
- 34) Dong, W., and Willett, K.L. 2008. Local expression of CYP19A1 and CYP19A2 in developing and adult killifish (*Fundulus heteroclitus*). *General and Comparative Endocrinology*. 155: 307-317.
- 35) Zhu, S., Li, L., Thornton, C., Carvalho, P., Avery, B.A., and Willett, K.L. 2008. Simultaneous determination of benzo[a]pyrene and eight of its metabolites in *Fundulus heteroclitus* bile using ultra performance liquid chromatography with mass spectrometry. *Journal of Chromatography B*. 863:141-149.
- 36) Dong, W., Wang, L., Thornton, C., Scheffler, B.E., and Willett, K.L. 2008. Benzo(a)pyrene decreases brain and ovarian aromatase mRNA expression. *Aquatic Toxicology*. 88:289-300.
- 37) Wills, L.P., Zhu, S., Willett, K.L., and Di Giulio, R.T. 2009. Effect of CYP1A inhibition on the biotransformation of benzo(a)pyrene in two populations of *Fundulus heteroclitus* with different exposure histories. *Aquatic Toxicology*. 92:195-201.
- 38) Hu, Y, Willett, K.L., Khan, I.A., Scheffler, B.E., and Dasmahapatra, A.K. 2009. Ethanol disrupts chondrification of the neurocranial cartilages in medaka embryos without affecting aldehyde dehydrogenase 1A2 (Aldh1A2) promoter methylation. *Comparative Biochemistry and Physiology Part C*. 150(4):495-502.
- 39) Singh, S.P., Azua, A., Chaudhary, A., Khan, S., Willett, K.L., and Gardinali, P. 2010. Occurrence and distribution of steroids, hormones and selected pharmaceuticals in South Florida coastal environments. *Ecotoxicology*. 19:338-350.
- 40) Kasimsetty, S.G., Bialonska, D., Reddy, M.K., Thornton, C., Willett, K.L., and Ferreira, D. 2009. Effects of pomegranate chemical constituents/intestinal microbial metabolites on CYP1B1 in 22Rv1 prostate cancer cells. *Journal of Agricultural and Food Chemistry*. 57(22):10636-10644.
- 41) Fang, X., Dong, W., Thornton, C., Scheffler, B., and Willett, K.L. 2010. Benzo(a)pyrene-induced glycine N-methyltransferase messenger RNA expression in *Fundulus heteroclitus* embryos. *Marine Environmental Research*. In press.

- 42) Weston, J., Warren, C., Chaudhary, A., Emerson, B., Argote, K., Khan, S., and Willett, K.L. 2010. Use of bioassays and sediment PAH concentrations to predict toxicity at coastal Hurricane Katrina impacted sites. *Environmental Toxicology and Chemistry*. 29(7):1409-1418.
- 43) Duzgoren-Aydin, N.S., Avula, B., Willett, K.L. and Khan, I.A. 2010. Determination of solid-bound trace element concentrations using collision/reaction cell inductively coupled plasma-mass spectrometry. *Environmental Monitoring and Assessment*. In press.
- 44) Scornaienchi, M.L., Thornton, C., Willett, K.L., and Wilson, J.Y. 2010. Cytochrome P450 mediated 17 $\beta$ -estradiol metabolism in zebrafish (*Danio rerio*) using a heterologous expression system. *Journal of Endocrinology*. In press.
- 45) Wang, L., Camus, A., Thornton, C., and Willett, K.L. 2010. Role of CYP1C1 and CYP1A in PAH-induced carcinogenesis in a fish model: *Fundulus heteroclitus*. *Aquatic Toxicology*. In press.
- 46) Fang, X., Dong, W., Thornton, C., and Willett, K.L. 2010. Benzo[a]pyrene increases glycine N-methyltransferase mRNA expression but decreases enzyme activity in *Fundulus heteroclitus* embryos. *Aquatic Toxicology* 98:130-138.
- 47) Scornaienchi, M.L., Thornton, C., Willett, K.L., and Wilson, J.Y. 2010. Functional differences in the cytochrome P450 1 family enzymes from zebrafish (*Danio rerio*) using heterologously expressed proteins. *Archives of Biochemistry and Biophysics*. In press.
- 48) Wills, L.P., Jung, D., Koehn, K., Zhu, S., Willett, K.L., Hinton, D.E. and Di Giulio, R.T. 2010. Comparative chronic liver toxicity of benzo[a]pyrene in two populations of the Atlantic killifish (*Fundulus heteroclitus*) with different exposure histories. *Environmental Health Perspectives*. In press.
- 49) Warren, C., Duzgoren-Aydin, N.S., Weston, J., and Willett, K.L. Trace element concentration in surface estuarine and marine sediments along the Mississippi gulf coast following Hurricane Katrina. Submitted to *Environmental Monitoring and Assessment*.

## C. Research Support

### Ongoing Research Support

R01 ES012710 Willett (PI)

Period: 7/1/04 – 8/31/10

NIEHS

Roles of CYP1 & 19 in *Fundulus* steroid & PAH metabolism

Role: PI

The hypothesis guiding this research is that CYP1B and/or CYP19 are involved in the molecular mechanisms of BaP toxicity. We expect that BaP exposure will alter both CYP1 and CYP19 gene regulation which, in turn, will be correlated with relevant reproductive / developmental and carcinogenic consequences. The goal is to gain insight into the mechanisms of action of PAHs and further validate *Fundulus* as a model organism in studies of PAH-mediated diseases.

R03AA016915 Dasmahapatra (PI)

Period: 7/15/07 – 6/30/10

NIAAA

Ethanol action in Japanese medaka: Alteration in specific gene methylation

Role: Co-PI

The primary focus of the project is to study the effects of ethanol on ALDH1A2 gene expression in Japanese medaka embryogenesis and to determine whether alteration in the methylation pattern of the CpG island in the promoter region of this gene is a possible cause for ethanol teratogenesis. Also the preventative potential of kudzu extracts will be investigated.

BAA #08-4383 Willett (PI)

Period: 2/1/09 – 9/30/2011

US Army Engineer Research and Development Center, EL-5

Distribution, bioaccumulation and toxicity of nanosilver particles in medaka (*Oryzias latipes*)

Role: PI

This project will provide critical data for assessing the environmental risk associated with silver nanoparticle use and potential release. Medaka will be used to understand how nanosilver particles absorb/accumulate and distribute in a living organism and their fate and toxicity in the fish.

NA07OAR4300494 Am. 2 Willett and Rimoldi (CoPI)

Period: 10/01/2003 – 09/30/10

NOAA-National Institute of Undersea Science and Technology

Seagrass Proteomics ; Profiling and Surveillance in the Gulf of Mexico

Role: Co-PI

The major goal of this project is to develop a working model of seagrass community response to multiple stressors that can be used in a predictive manner to estimate effects across seagrass communities in the northern Gulf of Mexico.