

EPA Risk-e-Learning webinar
“Ecological Risk: New Tools and Approaches”

Seminar title: "PAH and PCB Toxicity and Adaptation - Lessons Learned from Chronically Exposed Wild Populations"

**“Mechanisms of Evolved Resistance to Dioxin-like PCBs
in Fish Inhabiting a Marine Superfund Site”**

Mark E. Hahn
Woods Hole Oceanographic Institution

**References cited and other key papers on resistance adaptations
in *Fundulus heteroclitus* in New Bedford Harbor.**

- Bello, S. M., Franks, D. G., Stegeman, J. J., and Hahn, M. E. (2001). Acquired resistance to aryl hydrocarbon receptor agonists in a population of *Fundulus heteroclitus* from a marine Superfund site: In vivo and in vitro studies on the induction of xenobiotic-metabolizing enzymes. *Toxicol Sci* **60**, 77-91.
- Billiard, S. M., Timme-Laragy, A. R., Wassenberg, D. M., Cockman, C., and Di Giulio, R. T. (2006). The role of the aryl hydrocarbon receptor pathway in mediating synergistic developmental toxicity of polycyclic aromatic hydrocarbons to zebrafish. *Toxicol Sci* **92**, 526-536.
- Binder, R. L., and Stegeman, J. J. (1980). Induction of aryl hydrocarbon hydroxylase activity in embryos of an estuarine fish. *Biochem. Pharm.* **29**, 949-951.
- Bozinovic, B., and Oleksiak, M. F. (2010). Embryonic gene expression among pollutant resistant and sensitive *Fundulus heteroclitus* populations. *Aquat Toxicol* **98**, 221-229.
- Burnett, K. G., Bain, L. J., Baldwin, W. S., Callard, G. V., Cohen, S., Di Giulio, R. T., Evans, D. H., Gómez-Chiarri, M., Hahn, M. E., Hoover, C. A., Karchner, S. I., Katoh, F., MacLatchy, D. L., Marshall, W. S., Meyer, J. N., Nacci, D. E., Oleksiak, M. F., Rees, B. B., Singer, T. P., Stegeman, J. J., Towle, D. W., Veld, P. A. V., Vogelbein, W. K., Whitehead, A., Winn, R. N., and Crawford, D. L. (2007). Fundulus as the premier teleost model in environmental biology: Opportunities for new insights using genomics. *Comparative Biochemistry and Physiology* **D2**, 257-286.
- Burns, K. A. (1976). Microsomal mixed function oxidases in an estuarine fish, *Fundulus heteroclitus*, and their induction as a result of environmental contamination. *Comp. Biochem. Physiol.* **53B**, 443-446.
- Clark, B. W., Matson, C. W., Jung, D., and Di Giulio, R. T. (2010). AHR2 mediates cardiac teratogenesis of polycyclic aromatic hydrocarbons and PCB-126 in Atlantic killifish (*Fundulus heteroclitus*). *Aquat Toxicol* **99**, 232-240.
- Cohen, S. (2002). Strong positive selection and habitat-specific amino acid substitution patterns in MHC from an estuarine fish under intense pollution stress. *Molecular biology and evolution* **19**, 1870-1880.
- Fisher, M. A., and Oleksiak, M. F. (2007). Convergence and divergence in gene expression among natural populations exposed to pollution. *BMC genomics* **8**, 108.
- Greytak, S. R., and Callard, G. V. (2007). Cloning of three estrogen receptors (ER) from killifish (*Fundulus heteroclitus*): Differences in populations from polluted and reference environments. *Gen Comp Endocrinol* **150**, 174-188.
- Greytak, S. R., Champlin, D., and Callard, G. V. (2005). Isolation and characterization of two cytochrome P450 aromatase forms in killifish (*Fundulus heteroclitus*): differential expression in fish from polluted and unpolluted environments. *Aquat Toxicol* **71**, 371-389.
- Greytak, S. R., Tarrant, A. M., Nacci, D., Hahn, M. E., and Callard, G. V. (2010). Estrogen responses in killifish (*Fundulus heteroclitus*) from polluted and unpolluted environments are site- and gene-specific. *Aquat Toxicol* **99**, 291-299.
- Hahn, M. E., Karchner, S. I., Franks, D. G., and Merson, R. R. (2004). Aryl hydrocarbon receptor polymorphisms and dioxin resistance in Atlantic killifish (*Fundulus heteroclitus*). *Pharmacogenetics* **14**, 131-143.

- Hahn, M. E., Karchner, S. I., Shapiro, M. A., and Perera, S. A. (1997). Molecular evolution of two vertebrate aryl hydrocarbon (dioxin) receptors (AHR1 and AHR2) and the PAS family. *Proceedings of the National Academy of Sciences U.S.A.* **94**, 13743-13748.
- Head, J. A., Hahn, M. E., and Kennedy, S. W. (2008). Key amino acids in the aryl hydrocarbon receptor predict dioxin sensitivity in avian species. *Environmental science & technology* **42**, 7535-7541.
- Karchner, S. I., Franks, D. G., and Hahn, M. E. (2005). AHR1B, a new functional aryl hydrocarbon receptor in zebrafish: tandem arrangement of *ahr1b* and *ahr2* genes. *Biochemical Journal* **392**, 153-161.
- Karchner, S. I., Franks, D. G., Kennedy, S. W., and Hahn, M. E. (2006). The molecular basis for differential dioxin sensitivity in birds: Role of the aryl hydrocarbon receptor. *Proc Natl Acad Sci U S A* **103**, 6252-6257.
- Karchner, S. I., Franks, D. G., Powell, W. H., and Hahn, M. E. (2002). Regulatory interactions among three members of the vertebrate aryl hydrocarbon receptor family: AHR repressor, AHR1, and AHR2. *The Journal of biological chemistry* **277**, 6949-6959.
- Karchner, S. I., Powell, W. H., and Hahn, M. E. (1999). Identification and functional characterization of two highly divergent aryl hydrocarbon receptors (AHR1 and AHR2) in the teleost *Fundulus heteroclitus*. Evidence for a novel subfamily of ligand-binding basic helix-loop-helix Per-ARNT-Sim (bHLH-PAS) factors. *J Biol Chem* **274**, 33814-33824.
- Matson, C. W., Clark, B. W., Jenny, M. J., Fleming, C. R., Hahn, M. E., and Di Giulio, R. T. (2008). Development of the morpholino gene knockdown technique in *Fundulus heteroclitus*: a tool for studying molecular mechanisms in an established environmental model. *Aquat Toxicol* **87**, 289-295.
- Mitton, J. B., and Koehn, R. K. (1975). Genetic organization and adaptive response of allozymes to ecological variables in *Fundulus heteroclitus*. *Genetics* **79**, 97-111.
- Morrison, H. G., Weil, E. J., Karchner, S. I., Sogin, M. L., and Stegeman, J. J. (1998). Molecular cloning of CYP1A from the estuarine fish *Fundulus heteroclitus* and phylogenetic analysis of CYP1A genes: Update with new sequences. *Comparative Biochemistry and Physiology* **121C**, 231-240.
- Nacci, D. E., Champlin, D., and Jayaraman, S. (2010). Adaptation of the estuarine fish *Fundulus heteroclitus* (Atlantic killifish) to polychlorinated biphenyls (PCBs). *Estuaries and Coasts* **33**, 853-864.
- Nacci, D. E., Champlin, D., Coiro, L., McKinney, R., and Jayaraman, S. (2002). Predicting the occurrence of genetic adaptation to dioxinlike compounds in populations of the estuarine fish *Fundulus heteroclitus*. *Environmental Toxicology and Chemistry* **21**, 1525-1532.
- Nacci, D., Coiro, L., Champlin, D., Jayaraman, S., McKinney, R., Gleason, T., Munns Jr, W. R., Specker, J. L., and Cooper, K. (1999). Adaptation of wild populations of the estuarine fish *Fundulus heteroclitus* to persistent environmental contaminants. *Marine Biology* **134**, 9-17.
- Nacci, D., Coiro, L., Kuhn, A., Champlin, D., Munns Jr, W., Specker, J., and Cooper, K. (1998). A non-destructive indicator of EROD activity in embryonic fish. *Environmental Toxicology and Chemistry* **17**, 2481-2486.
- Nacci, D., Huber, M., Champlin, D., Jayaraman, S., Cohen, S., Gauger, E., Fong, A., and Gomez-Chiarri, M. (2009). Evolution of tolerance to PCBs and susceptibility to a bacterial pathogen (*Vibrio harveyi*) in Atlantic killifish (*Fundulus heteroclitus*) from New Bedford (MA, USA) harbor. *Environ Pollut* **157**, 857-864.
- Oleksiak, M. F. (2008). Changes in gene expression due to chronic exposure to environmental pollutants. *Aquat Toxicol* **90**, 161-171.
- Oleksiak, M. F., Churchill, G. A., and Crawford, D. L. (2002). Variation in gene expression within and among natural populations. *Nature genetics* **32**, 261-266.
- Oleksiak, M. F., Kolell, K. J., and Crawford, D. L. (2001). Utility of natural populations for microarray analyses: Isolation of genes necessary for functional genomic studies. *Marine Biotechnology* **3**, S203-S211.
- Powell, W. H., and Hahn, M. E. (2002). Identification and Functional Characterization of Hypoxia-inducible factor 2a from the estuarine teleost, *Fundulus heteroclitus*: Interaction of HIF-2a with two ARNT2 splice variants. *J. Exp. Zool. (Mol. Dev. Evol.)* **294**, 17-29.
- Powell, W. H., Bright, R., Bello, S. M., and Hahn, M. E. (2000). Developmental and tissue-specific expression of AHR1, AHR2, and ARNT2 in dioxin-sensitive and -resistant populations of the marine fish, *Fundulus heteroclitus*. *Toxicol Sci* **57**, 229-239.
- Powell, W. H., Karchner, S. I., Bright, R., and Hahn, M. E. (1999). Functional diversity of vertebrate ARNT proteins: Identification of ARNT2 as the predominant form of ARNT in the marine teleost, *Fundulus heteroclitus*. *Arch Biochem Biophys* **361**, 156-163.
- Powell, W. H., Morrison, H. G., Weil, E. J., Karchner, S. I., Sogin, M. L., Stegeman, J. J., and Hahn, M. E. (2004).

- Cloning and analysis of the CYP1A promoter from the Atlantic killifish (*Fundulus heteroclitus*). *Mar Environ Res* **58**, 119-124.
- Powers, D. A., and Schulte, P. M. (1998). Evolutionary adaptations of gene structure and expression in natural populations in relation to a changing environment: a multidisciplinary approach to address the million-year saga of a small fish. *The Journal of experimental zoology* **282**, 71-94.
- Powers, D., and Place, A. (1978). Geographical variations in temperature effects on enzymes of Fundulus. *Biochemical Genetics* **16**, 593-607.
- Prince, R., and Cooper, K. R. (1995). Comparisons of the effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on chemically impacted and nonimpacted subpopulations of *Fundulus heteroclitus*: I. TCDD toxicity. *Environmental Toxicology and Chemistry* **14**, 579-587.
- Prince, R., and Cooper, K. R. (1995). Comparisons of the effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on chemically impacted and nonimpacted subpopulations of *Fundulus heteroclitus*: II. Metabolic considerations. *Environmental Toxicology and Chemistry* **14**, 589-595.
- Stegeman, J. J. (1978). Influence of environmental contamination on cytochrome P-450 mixed-function oxygenases in fish: implications for recovery in the Wild Harbor Marsh. *J. Fish. Res. Bd. Can.* **35**, 668-674.
- van Veld, P. A., and Nacci, D. E. (2007). Chapter 13. Toxicity Resistance. In *The Toxicology of Fishes* (R. T. Di Giulio, and D. E. Hinton, Eds.). Taylor & Francis.
- Wang, L., Scheffler, B. E., and Willett, K. L. (2006). CYP1C1 mRNA Expression is Inducible by Benzo(a)pyrene in *Fundulus heteroclitus* Embryos and Adults. *Toxicol Sci* **93**, 331-340.
- Weis, J. S., Heber, M., Weis, P., and Vaidya, S. (1981). Methylmercury tolerance of killifish (*Fundulus heteroclitus*) embryos from a polluted vs non-polluted environment. *Mar. Biol.* **65**, 283-287.
- Whitehead, A., Triant, D. A., Champlin, D., and Nacci, D. (2010). Comparative transcriptomics implicates mechanisms of evolved pollution tolerance in a killifish population. *Molecular ecology*, in press.
- Whitehead, A., Galvez, F., Zhang, S., Williams, L. M., and Oleksiak, M. F. (2010). Functional genomics of physiological plasticity and local adaptation in killifish. *Journal of Heredity*, in press.
- Williams, L. M., and Oleksiak, M. F. (2008). Signatures of selection in natural populations adapted to chronic pollution. *BMC evolutionary biology* **8**, 282.
- Williams, L. M., Ma, X., Boyko, A. R., Bustamante, C. D., and Oleksiak, M. F. (2010). SNP identification, verification, and utility for population genetics in a non-model genus. *BMC genetics* **11**, 32.
- Wirgin, I., and Waldman, J. R. (2004). Resistance to contaminants in North American fish populations. *Mutation research* **552**, 73-100.
- Woods, R., and Hoffman, A. (2000). Chapter 9: Evolution in Toxic Environments: Quantitative Versus Major Gene Approaches. In *Demography in Ecotoxicology* (J. Kammenga, and R. Laskowski, Eds.). Wiley.
- Zanette, J., Jenny, M. J., Goldstone, J. V., Woodin, B. R., Watka, L. A., Bainy, A. C., and Stegeman, J. J. (2009). New cytochrome P450 1B1, 1C2 and 1D1 genes in the killifish *Fundulus heteroclitus*: Basal expression and response of five killifish CYP1s to the AHR agonist PCB126. *Aquat Toxicol* **93**, 234-243.