



## Superfund Research Program

The Superfund Research Program (SRP) supports practical research that creates benefits, such as lower environmental cleanup costs and reduced risk of exposure to hazardous substances, to improve human health. SRP funds colleges, universities, and small businesses, including the University of Washington Superfund Research Center (UW SRC), to advance this work across the nation.

### Research Highlights



Furlong and his team are working to understand possible protective effects of paraoxonase enzymes, including PON2, in brain toxicity and cardiovascular diseases. (Photo courtesy of Jim Rice)

#### Protecting brain cells from metal toxicity

The enzyme paraoxonase-2 (PON2) may protect brain cells from damage, and lower PON2 levels in males may contribute to greater susceptibility to neurotoxicity, or damage to the nervous system, according to recent UW SRC findings.<sup>1</sup> PON2 is an enzyme found in cells that helps protect them from toxic effects of a cellular process called oxidative stress.<sup>2</sup> Oxidative stress can contribute to numerous problems, such as inflammation, neurotoxicity, and cardiovascular disease.

Clement Furlong, Ph.D., and his collaborators found that PON2 levels in brains of male mice were lower than in females. They tested whether

PON2 levels affected neurotoxicity, and found that male brain cells were more susceptible to the toxic effects of oxidative stress than female brain cells.<sup>1</sup> Treatment of brain cells with the female hormone estradiol increased PON2 levels and protected brain cells from oxidative stress toxicity. Furlong and his team are now studying how PON2 affects neurotoxicity after exposure to cadmium and manganese, two metals found in food and air as a result of industrial processes and burning of fossil fuels.<sup>3,4,5</sup> PON2 may be a useful biological indicator, or biomarker, of susceptibility to environmental chemicals. This information may also help researchers find ways to reduce cellular damage associated with oxidative stress in Parkinson's disease and cardiovascular disease.

#### Copper exposure and olfactory injury in fish

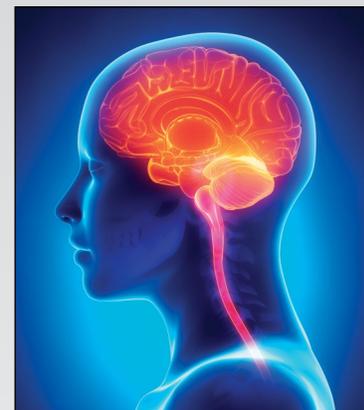
Environmental metals, such as copper, can disrupt olfactory function, or the sense of smell, in fish. The olfactory system is critical to survival, because fish rely on their sense of smell for homing, predator avoidance, and reproduction.

UW SRC researchers identified micro-ribonucleic acids (miRNAs) in the zebrafish olfactory system that were produced following exposure to copper, providing a clue to copper-induced neurotoxicity pathways in fish.<sup>6</sup> These miRNAs can disrupt how genes regulate the nervous system. This finding may explain how injury to the olfactory system occurs. It may also indicate when exposure to copper has occurred.

Evan Gallagher, Ph.D., and his team found other differences in how miRNAs are expressed with increasing exposure of zebrafish to copper in water. They are now studying these miRNAs in detail to understand cellular processes involved in the toxic responses.



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UW SRC researchers are identifying biomarkers that may help predict who may be more susceptible to metals. Researchers are also investigating how exposures harm the nervous and olfactory systems in humans and fish.

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## Working with a community coalition to address pollution concerns

Tom Burbacher, Ph.D., and the UW SRC Community Engagement Core have been partnering with the Northwest Toxic Communities Coalition since 2005. More than 40 organizations are collaborating, through the coalition, to help address concerns about local hazardous waste sites and air pollution in the Pacific Northwest. UW SRC, the U.S. Environmental Protection Agency (EPA), community groups, and environmental and social justice organizations share information and strategies for addressing environmental problems. UW SRC has also worked closely with these partners to improve information access to communities directly impacted by hazardous waste sites.

One local concern is the Duwamish River. The river is contaminated with more than 40 substances, including polycyclic aromatic hydrocarbons and arsenic, both of which cause cancer.<sup>7</sup> Through community forums and outreach, UW SRC is educating the Seattle community and local tribes about the cleanup plan for the Duwamish River, and the types of Duwamish River fish and shellfish that do not absorb high levels of pollutants, and can, therefore, be consumed safely.



A 1/2 mile stretch of the lower Duwamish River is a Superfund site where the EPA is cleaning up contaminants. (Photo courtesy of University of Washington)

## The importance of studying biomarkers

Biomarkers are biological indicators of physiological functions in cells and organisms. Biomarkers include proteins, enzymes, DNA, and other cellular chemicals that can change under specific conditions. Depending on the biomarker, researchers and physicians are alerted to conditions, such as exposure to environmental chemicals, problems with cellular or organ functions, or special susceptibilities to diseases or damage from toxic agents. UW SRC researchers focus on using biomarkers to monitor the nervous system in humans, as well as aquatic ecosystem health.<sup>8,9</sup>

## Research overview

- Determining how exposure to cadmium harms the olfactory system and affects the behavior of Pacific salmon and zebrafish. (Evan Gallagher, Ph.D., [evang3@uw.edu](mailto:evang3@uw.edu))
- Studying how cadmium affects brain functions at the cellular and molecular level. (Zhengui Xia, Ph.D., [zxia@uw.edu](mailto:zxia@uw.edu))
- Evaluating the role of paraoxonases, including PON2, in preventing nervous system toxicity after exposure to cadmium and manganese. (Clement Furlong, Ph.D., [clem@uw.edu](mailto:clem@uw.edu))
- Studying arsenic mobility in the environment, and its accumulation in living organisms in lakes in Washington state. (Rebecca Neumann, Ph.D., [rbneum@uw.edu](mailto:rbneum@uw.edu))

## Sharing results

- UW SRC is advancing science by partnering with government agencies, promoting use of their scientific tools and methods at contaminated sites, and facilitating application of research results to improve public health. (Thomas Burbacher, Ph.D., [tmb@uw.edu](mailto:tmb@uw.edu))
- UW SRC works directly with community groups associated with hazardous waste sites, supports the Northwest Toxic Communities Coalition, and assists federal, state, and local agencies in communicating with communities. (Thomas Burbacher, Ph.D., [tmb@uw.edu](mailto:tmb@uw.edu))

## Other contributions to advance science

- The UW SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Federico Farin, M.D., [freddy@uw.edu](mailto:freddy@uw.edu))
- The UW SRC integrated, multidisciplinary training experience provides early-career scientists access to teams of diverse professionals, and encourages innovation to develop solution-oriented approaches to complex environmental health problems. (Evan Gallagher, Ph.D., [evang3@uw.edu](mailto:evang3@uw.edu))

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For more information on the National Institute of Environmental Health Sciences, visit [www.niehs.nih.gov](http://www.niehs.nih.gov).

For more information on the Superfund Research Program, visit [www.niehs.nih.gov/srp](http://www.niehs.nih.gov/srp).

For more information on the University of Washington Superfund Research Center, visit <http://depts.washington.edu/sfund>.

<sup>1</sup> Giordano G, Tait L, Furlong CE, Cole TB, Kavanagh TJ, Costa LG. 2013. Gender differences in brain susceptibility to oxidative stress are mediated by levels of paraoxonase-2 expression. *Free Radic Biol Med* 58:98-108.

<sup>2</sup> Costa LG, de Laat R, Dao K, Pellacani C, Cole TB, Furlong CE. 2014. Paraoxonase-2 (PON2) in brain and its potential role in neuroprotection. *Neurotoxicology* 43:3-9.

<sup>3</sup> NIEHS (National Institute of Environmental Health Sciences). 2015. University of Washington Superfund Research Program: Role of Paraoxonases (PONs) in Modulating Neurotoxicity. Available: [https://tools.niehs.nih.gov/srp/programs/Program\\_detail.cfm?Project\\_ID=P42ES46960103](https://tools.niehs.nih.gov/srp/programs/Program_detail.cfm?Project_ID=P42ES46960103) [accessed 4 January 2016].

<sup>4</sup> EPA (U.S. Environmental Protection Agency). 2015. Cadmium Compounds. Available: <http://www3.epa.gov/airtoxics/hlthef/cadmium.html> [accessed 9 February 2016].

<sup>5</sup> EPA (U.S. Environmental Protection Agency). 2015. Manganese Compounds. Available: <http://www3.epa.gov/airtoxics/hlthef/manganes.html> [accessed 9 February 2016].

<sup>6</sup> Wang L, Bammler TK, Beyer RP, Gallagher EP. 2013. Copper-induced deregulation of microRNA expression in the zebrafish olfactory system. *Environ Sci Technol* 47(13):7466-7474.

<sup>7</sup> EPA (U.S. Environmental Protection Agency). 2013. EPA proposes plan to clean up Lower Duwamish Waterway from decades of industrial pollution. Available: <http://yosemite.epa.gov/opa/admpress.nsf/652d9edd5cf71a2585257359003f5343/a2d787f8db15928c85257b2000650ad3?OpenDocument> [accessed 10 February 2016].

<sup>8</sup> University of Washington Superfund Research Program. 2015. Effects-Related Biomarkers of Environmental Neurotoxic Exposures. Available: <http://depts.washington.edu/sfund> [accessed 4 January 2016].

<sup>9</sup> Hook SE, Gallagher EP, Batley GE. 2014. The role of biomarkers in the assessment of aquatic ecosystem health. *Integr Environ Assess Manag* 10(3):327-341.