

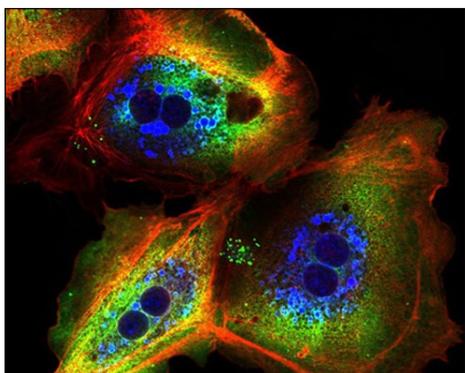


Superfund Research Program

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 California, San Diego Superfund Research Center (UCSD SRC), to advance this work across the nation.

Research Highlights

Linking exposures to liver disease and cancer

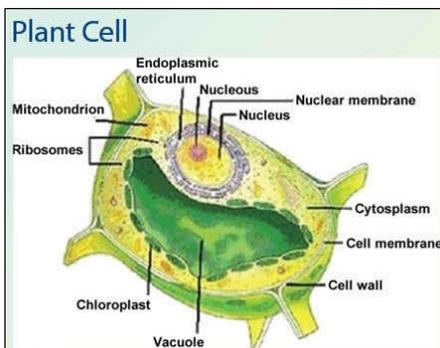


Karin's work shows how liver cells become cancerous after exposure to carcinogenic chemicals. (Photo courtesy of UCSD SRC)

The antibacterial chemical triclosan, which is added to many personal care products, such as hand soap, can promote liver tumor formation in mice, according to University of California, Davis and UCSD SRC research.¹ Michael Karin, Ph.D., and Robert Tukey, Ph.D., collaborated as part of their work to understand the effects of hazardous substances on liver function and cancer. They reported that triclosan exposure alone resulted in increased numbers of liver cells, increased liver damage, and decreased liver function. When mice were exposed to triclosan and the cancer-causing agent diethylnitrosamine (DEN) together, more mice had liver tumors and their tumors were larger compared to mice exposed to DEN alone.¹ Karin's UCSD SRC team also identified liver cells that were precancerous. They are using these cells to increase understanding of how normal cells become cancer cells, using genetic and biochemical approaches.²

Metal uptake in seeds and leaves of plants

The UCSD SRC team, led by Julian Schroeder, Ph.D., identified a gene that regulates how much of different metals accumulate in the seeds and leaves of plants.³ Some metals are important nutrients, like zinc and iron, but other metals, like cadmium, can be toxic to humans.⁴ This information may help scientists modify plants so they can absorb more metals from contaminated soil or water and be used as a tool for cleaning up Superfund sites. Researchers may also be able to reduce metal accumulation in plants to prevent exposures to metals that are present in certain foods, such as arsenic in rice.⁵



Schroeder's team is studying how metals accumulate in plant cells. (Photo courtesy of UCSD SRC)

UC San Diego



The UCSD SRC interdisciplinary team seeks to better understand molecular processes that cause health problems for people exposed to environmental contaminants, and works to improve contaminant detection, monitoring, and cleanup. They also work to solve problems that are unique to California's coastal environment and the densely populated U.S.-Mexico border region.

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A community garden as a living laboratory

Keith Pezzoli, Ph.D., and his team are working with the nonprofit Global Action Research Center to transform a vacant 20,000 square foot lot into a community garden and platform for environmental health education called the Ocean View Growing Grounds (OVGG).⁶ The lot in southeast San Diego is a brownfield site, which is previously-owned land that may contain hazardous substances. OVGG participants are working with UCSD SRC scientists and the city of San Diego to do environmental testing and develop strategies to clean up the site. The garden will transform one of San Diego's disadvantaged neighborhoods into a food forest and living laboratory to test soils and plants.



Pezzoli, right, is helping convert a brownfield into an urban garden in San Diego. (Photo courtesy of UCSD SRC)

The importance of studying environmental contaminants

- Liver cancer was the fifth most frequently diagnosed cancer in 2010, with an estimated 23,000 deaths in 2014.⁷
- Cadmium and arsenic exposures are associated with cancer, cardiovascular disease, lung disease, and other adverse health effects.^{4,8}

Research overview

- Understanding genetic susceptibilities to arsenic and cadmium toxicity. (Paul Russell, Ph.D., prussell@scripps.edu)
- Researching protective effects of natural antioxidants in arsenic-induced liver disease. (Robert Tukey, Ph.D., rtukey@ucsd.edu)
- Understanding how pre-existing liver disease affects sensitivity to toxicant exposures. (David Brenner, Ph.D., dbrenner@ucsd.edu)
- Understanding effects of toxicants on precancerous liver cells and liver cancer, and how normal cells become cancer cells. (Michael Karin, Ph.D., karinoffice@ucsd.edu)
- Developing field-portable devices to detect hormone-disrupting and cancer-causing chemicals. (William Trogler, Ph.D., wtrogler@ucsd.edu)
- Investigating heavy metal uptake and detoxification in plants used for cleanup. (Julian Schroeder, Ph.D., jischroeder@ucsd.edu)
- Studying how Superfund contaminants affect cellular functions, and how changes are linked to health problems. (Ronald Evans, Ph.D., evans@salk.edu)

Sharing results

- UCSD SRC works with the San Diego-Tijuana community, providing environmental health and scientific research information. In turn, researchers learn about community needs that may help guide future research. (Keith Pezzoli, Ph.D., kpezzoli@ucsd.edu)

Other contributions to advance science

- The UCSD SRC research support facility provides vital access to expertise, research resources, and state-of-the-art instrumentation for its research projects. (Pamela Mellon, Ph.D., pmellon@ucsd.edu; Mark Ellisman, Ph.D., mellisman@ucsd.edu)
- The UCSD 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. (Pamela Mellon, Ph.D., pmellon@ucsd.edu)

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For more information on the National Institute of Environmental Health Sciences, visit www.niehs.nih.gov.

For more information on the Superfund Research Program, visit www.niehs.nih.gov/srp.

For more information on the University of California, San Diego Superfund Research Center, visit <http://superfund.ucsd.edu>.

¹ Yueh MF, Taniguchi K, Chen S, Evans RM, Hammock BD, Karin M, Tukey RH. 2014. The commonly used antimicrobial additive triclosan is a liver tumor promoter. *Proc Natl Acad Sci U S A* 111(48):17200-17205.

² He G, Dhar D, Nakagawa H, Font-Burgada J, Ogata H, Jiang Y, Shalpour S, Seki E, Yost S, Jepsen K, Frazer K, Harismendy O, Hatzia Apostolou M, Iliopoulos D, Suetsugu A, Hoffman RM, Tateishi R, Koike K, Karin M. 2013. Identification of liver cancer progenitors whose malignant progression depends on autocrine IL-6 signaling. *Cell* 155(2):384-396.

³ Mendoza-Cozatl DG, Xie Q, Akmakjian GZ, Jobe TO, Patel A, Stacey MG, Song L, Demoin DW, Jurisson SS, Stacey G, Schroeder JI. 2014. OPT3 is a component of the iron-signaling network between leaves and roots and misregulation of OPT3 leads to an over-accumulation of cadmium in seeds. *Molec Plant* 7(9):1455-1469.

⁴ ATSDR (Agency for Toxic Substances & Disease Registry). 2008. Cadmium Toxicity: What Diseases Are Associated With Chronic Exposure to Cadmium? Available: www.atsdr.cdc.gov/csem/csem.asp?csem=6&po=12 [accessed 1 June 2015].

⁵ Khan MA, Castro-Guerrero N, Mendoza-Cozatl DG. 2014. Moving toward a precise nutrition: preferential loading of seeds with essential nutrients over non-essential toxic elements. *Front Plant Sci* 5:51.

⁶ University of California, San Diego Superfund Research Center. 2014. New Plant Science Program for Urban Agriculture. Available: <http://superfund.ucsd.edu/news/plant-testing-program> [accessed 1 June 2015].

⁷ Siegel R, Ma J, Zou Z, Jemal A. 2014. Cancer statistics, 2014. *CA Cancer J Clin* 64(1):9-29.

⁸ Naujokas MF, Anderson B, Ahsan H, Aposhian HV, Graziano JH, Thompson C, Suk WA. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295-302.