

NTP postdoc takes top prize at NCSOT meeting

By Eddy Ball

The [North Carolina Chapter of the Society of Toxicology \(NCSOT\)](http://www.toxicology.org/isot/rc/nc/index.asp)

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held its annual fall meeting and awards ceremony for postdoctoral fellows Oct. 24 at NIEHS. The event featured presentations on the meeting theme, "From the Mountains to the Coast: Environmental Toxicology Research in North Carolina," by specialists from universities across the state.

Chaired by East Carolina University (ECU) toxicologist Jamie DeWitt, Ph.D., the meeting opened with presentation of the group's President's Award for Research Competition (PARC) to three area postdoctoral fellows, with first-place going [Yuanyuan \(Laura\) Xu, Ph.D.](#), a visiting fellow in the NTP Laboratories Inorganic Toxicology Group, headed by lead researcher Michael Waalkes, Ph.D.

In her winning abstract, Xu reported findings from a study on the contribution of inorganic arsenic exposure to the development of an important subset of breast cancers (see [text box](#)). Xu's award, her second PARC first place, included a monetary award and a place on the program.

Two postdoctoral fellows at the U.S. Environmental Protection Agency tied for second place. Samantha Snow, Ph.D., and Yong Ho Kim, Ph.D., also received cash prizes.

The main program, organized by chapter vice-president Christie Sayes, Ph.D., consisted of three talks on environmental health and ecological issues with specific relevance for the state of North Carolina. "We're branching a little away from the lab," DeWitt said of the program. "We went from the mountains with trees, to the coast with hurricanes, and finally to the piedmont and bees."

Environmental sustainability in Western Carolina

Western Carolina University forest ecology professor and Associate Dean of the Graduate School [Brian Kloepfel, Ph.D.](#),

(<http://paws.wcu.edu/bkloepfel/>)

gave the first presentation, which focused on watershed science. Kloepfel described natural and manmade changes to watersheds that impact the quantity and quality of the groundwater that makes up 96 percent of drinking water in the southeastern U.S.

According to Kloepfel, the combination of the upward temperature trend over the past 36 years and the devastation of the hemlock forest canopy over streams in western North Carolina through infestation by the woolly adelgid have resulted in higher water temperatures. Warmer water temperature in turn changes evaporation rates and makes water more hospitable to bacteria, with a potential impact on human health.

Coastal preservation in Eastern Carolina

Turning to the other end of the state, ECU organic geochemist [Siddhartha Mitra, Ph.D.](#),

(<http://siddharthamitra.com/>)

presented findings from his research on air and water quality. Mitra opened with a discussion of hurricanes and tropical storms and the transport of dissolved black and organic carbons in rainwater.

In one of his especially telling experiments, Mitra and colleagues measured the dramatic spike in carbon and oil-derived hydrocarbons in the wake of Tropical Storm Bonnie in 2010, which swept across the Gulf of Mexico following the Deepwater Horizon oil spill and dumped polluted rainwater on interior Louisiana. He said post-Bonnie air quality was comparable to conditions in the inner city.



Unfortunately, Xu was unable to attend the meeting and make the oral presentation that was part of her first prize win. Her colleague, NTP biologist Erik Tokar, Ph.D., accepted the award plaque on her behalf. (Photo courtesy of Steve McCaw)



During her report on chapter activities since the spring meeting and upcoming plans, DeWitt described NCSOT as one of the Society's most active chapters and one of its largest. Of its 428 members, 61 are postdocs and 82 are students. "I think that's phenomenal," DeWitt said. (Photo courtesy of Steve McCaw)

Carolina insect colony collapse

Although air and water quality can make headlines, the focus of studies by North Carolina State University professor [David Tarpy, Ph.D.](#),

(<http://www.cals.ncsu.edu/entomology/tarpy>)

has even made it into the tabloids and onto talk radio. The mysterious honeybee colony collapse disorder (CCD) became news in 2006 and inspired a media hysteria that has highlighted speculation about the causes.

After joking about some of the wilder notions - blaming CCD on divine rapture, terrorism, or a Russian plot - Tarpy suggested it's far more likely that a combination of factors is behind the sudden depopulation of hives. He said current studies are looking at how such factors as nutritional stress from transport; parasites and pathogens; and the complex chemical environment of beehives might work in synergy to alter bee behavior so suddenly and inexplicably that entire colonies disappear without a trace.



Kloepfel argued that an adequate supply of clean water is essential to sustainability. The best way to achieve that goal, he said, is through preventive maintenance of the distant forest and valleys that constitute the watershed. (Photo courtesy of Steve McCaw)



Tokar, right, was a coauthor on Xu's paper and a first-place PARC winner as a postdoctoral fellow in 2008 and 2009. (Photo courtesy of Steve McCaw)



PARC winners Snow, left, and Kim listened as DeWitt described the rigorous competition and the vote that resulted in a rare tie this year for second place. (Photo courtesy of Steve McCaw)



Mitra also presented findings from a study of onsite waste treatment systems as a potential source of pharmaceutical and personal care product pollution in water in eastern N.C. An estimated 85 percent of houses there are on septic systems and use wells for their water supply. (Photo courtesy of Steve McCaw)



"The ratio of chatter to data here is about a billion to one," Tarpay said of the rampant - and sometimes off the wall - speculation about what is causing CCD. (Photo courtesy of Steve McCaw)



As this reaction to one of Tarpay's quips by EPA biophysicist Carl Blackman, Ph.D., made clear, people in the audience were both edified and entertained by the dynamic speakers and the distinctive program. (Photo courtesy of Steve McCaw)

Making the connection between arsenic and breast cancer

For her prize-winning research, Xu built upon previous data suggesting that arsenic may be an endocrine disruptor and the association some studies have found between arsenic exposure and breast cancer. Through a series of experiments using the normal, estrogen receptor (ER)-negative breast epithelial cell line, MCF-10A, she and her colleagues built a convincing argument that arsenic induces an oncogenic phenotype and pinpointed a novel mechanism to explain the outcome through activation of aromatase.

The team subjected MCF-10A cells to continuous low level exposure to sodium arsenite over a 24-week period, producing what the researchers described as arsenic-transformed breast epithelial (ATBE) cells. They then compared ATBE to untreated control cells.

Xu reported significant to dramatic differences between ATBE and control cells for indices of oncogenicity and expression of critical genes relevant to breast cancer cells. ATBE cells showed increases over controls in colony formation (190 percent), secreted metalloproteinase (400 percent for MMP-9 and 290 percent for MMP-2), and proliferation rate (120 percent).

Expression of the tumor suppression genes p53 and PTEN was lowered by as much as 50 percent in ATBE cells. Other molecular markers and gene expression patterns for cancer cells were significantly abnormal compared to controls.

The researchers also observed widespread aromatase overexpression and marked increase in 17beta-estradiol, and established that the aromatase inhibitor letrozole was able to abolish 17beta estradiol increases and reverse the arsenic-induced oncogenic phenotype. The experiments provided evidence of transformation of breast epithelia through a process independent of ER, a process, they said, not previously considered.

Citation: Xu Y, Tokar EJ, Waalkes MP. 2013. Arsenic induces an oncogenic phenotype in human breast epithelia through an estrogen-receptor independent pathway by aromatase activation. NCSOT PARC abstract.

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