

NTP postdocs recognized with Society for Toxicologic Pathology awards

By Eddy Ball

NTP postdocs won two of the three Young Investigator Awards presented at this year's [Society of Toxicologic Pathology \(STP\)](http://www.toxpath.org/)

(<http://www.toxpath.org/>)

[annual meeting](http://www.toxpath.org/)

(<http://www.toxpath.org/am2013/>)

June 16-20 in Portland, Ore.

The NTP awardees are Sachin Bhusari, D.V.M., Ph.D., who placed first, and Michael Boyle, D.V.M., who placed third. Bhusari is a member of the Cellular and Molecular Pathology Branch (CMPB) Investigative Pathology Group, headed by pathologist [Mark Hoenerhoff, D.V.M., Ph.D.](#)

Boyle is part of the CMPB NTP Pathology Group, headed by pathologist [David Malarkey, D.V.M., Ph.D.](#), and is also being mentored in his Ph.D. research, on the modulation of chromatin-remodeling factors in cardiovascular development and disease, by NIEHS lead researcher Trevor Archer, Ph.D., head of the Laboratory of Molecular Carcinogenesis.

Kudos for the winners and for NTP

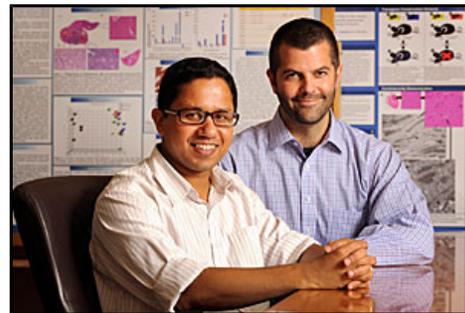
Both awardees earned high praise on the quality of their research and the impact that this research has on the scientific community (see [text box](#)) from their mentors, as well as from CMPB head Robert Sills, D.V.M., Ph.D. In addition to acknowledging the superior work by the trainees, Hoenerhoff said, "This award also reflects highly on the high standards of quality the NTP has achieved in terms of training and research."

"Ours is the only program of its kind in the U.S. and the world. Trainees learn rodent pathology, provide institute support, work on NTP projects, and prepare for board certification by the American College of Veterinary Pathologists (ACVP)," added Malarkey, who has been instrumental in establishing a formalized and successful NIEHS Toxicological Pathology Training Program. "There have been 13 pathology trainees in the program since 2003, with 11 becoming board-certified by the American College of Veterinary Pathologists (ACVP), and 4 simultaneously pursuing, or having received, a Ph.D. from NCSU [North Carolina State University]."

Well-deserved recognition

"Receiving first place in the Society of Toxicologic Pathology Young Investigator Awards is a very significant accomplishment for Dr. Bhusari," Hoenerhoff explained. "This award is one of many that he has been awarded during his time at NTP, and is really a testament to his dedication to toxicology and cancer research." Among Bhusari's earlier accomplishments was earning recognition as a Diplomate of the American Board of Toxicology (ABT), one of the profession's top certifications.

According to Malarkey, in addition to his work on NTP studies, Boyle also assists NIEHS intramural researchers in the design, implementation, and evaluation of animal studies. He is an ACVP board-certified veterinary pathologist, and currently pursuing certification by ABT, in addition to his Ph.D. research.



Bhusari, left, and Boyle were recognized by the world's leading professional organization in the advancement of pathology, as it pertains to changes elicited by pharmacological, chemical, or environmental agents, as well as factors that modify these responses. STP membership includes some 1,250 scientists and professionals in more than 28 countries. (Photo courtesy of Steve McCaw)

Award-winning research

- **Bhusari S**, Pandiri A, Wang Y, Foley J, Hong H-H, Ton TVT, Shockley K, Peddada S, Gerrish K, Malarkey D, Sills R, Hoenerhoff M. 2013. Transcriptomic Profiling of Hepatoblastomas and Associated Hepatocellular Carcinomas in B6C3F1 Mice. Unpublished meeting abstract.

A team of NTP and NIEHS researchers identified global transcriptomic changes in chemically induced hepatoblastomas (HB), associated hepatocellular carcinomas (HCC), tumor adjacent normal liver, and vehicle control liver to define gene expression patterns informative of the pathogenesis of HB in mice and its human relevance. Using frozen samples from a 2-year NTP bioassay in B6C3F1 mice that were laser capture microdissected, the team of scientists performed microarray analysis to identify differentially expressed genes between sample groups.

Transcriptomic analysis using Ingenuity Pathway Analysis revealed significant alterations in hepatic development and embryonic stem cell regulation, and genomic imprinting in HB compared to HCC. These genomic alterations were also relevant to the pathogenesis of human HB, and the findings point to a potential for more accurate assessment of chemically induced hepatocarcinogenesis and its human relevance in hazard identification.

- **Boyle MC**, Hoffman JA, Malarkey DE, Archer TK. 2013. Deletion of the Chromatin-Remodeling Factor Brg1 Confers Sensitivity to Doxorubicin Cardiotoxicity in Mice. Unpublished meeting abstract.

NTP Pathologists Boyle and Malarkey and NIEHS cancer biologists Hoffman and Archer conducted experiments involving chronic exposure of wild-type and Brg1 transgenic knockout (KO) mice to doxorubicin, a cancer chemotherapeutic known to produce cardiotoxicity, a primary or comorbid factor involved in cardiovascular disease. The engineered mice were the outcome of an inducible deletion of the chromatin-remodeling factor Brg1.

The researchers found lesions consistent with chronic anthracycline cardiotoxicity in all treated mice, including multifocal discrete sarcoplasmic vacuolar degeneration and multifocal sarcoplasmic fragmentation, but were increased in Brg1 KO mice. They concluded the increased number and severity of lesions observed in the Brg1 KO mice suggest genetic deletion of functional units of the chromatin-remodeling factor Brg1 confers sensitivity to cardiotoxicants. In addition, they postulated that the Brg1 KO mouse is a sensitive model of cardiotoxicity for risk assessment and hazard identification.

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