Zebrafish model may lead to new therapies for mitochondrial disease

By Monica Frazier

Sherine Chan, Ph.D.,
(http://academicdepartments.musc.edu/pharmacology/COBRE/Sherine%20Chan)
former NIEHS trainee and current assistant professor in the Department of Pharmaceutical and Biomedical Sciences at the Medical University of South Carolina (MUSC), spoke Nov. 15 at Duke University. Her presentation was part of the fall Integrated Toxicology and Environmental Health Program (ITEHP) seminar series.

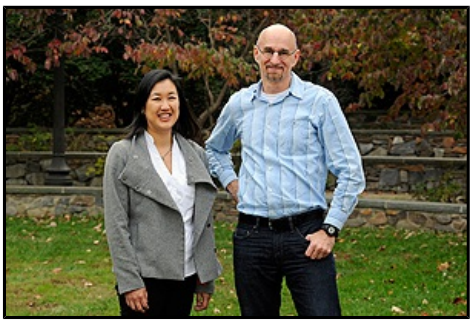
Chan responded to questions from her audience. (Photo courtesy of Steve McCaw)

Her talk on "Environmental Toxicant Exposures, Mitochondrial Dysfunction, and Birth Defects" attracted a capacity audience to the Levine Science Research Center at Duke, which houses ITEHP.

Chan, a former postdoc in the NIEHS Mitochondrial DNA Replication Group, has been at MUSC for more than 4 years, and has developed her own group to advance the mitochondrial research interests she developed during her time at NIEHS, which has potential applications in a range of diseases linked to defects in energy production (see text box).

The need for a new animal model of mitochondrial dysfunction

Chan opened her talk by saying, "The big problem with mitochondrial dysfunction is there are no cures, and there are no good treatments that are currently available on the market." As she went on to explain, "One of the reasons why that might be is that there are no good animal models [for drug discovery]."



Following her talk, Chan joined Copeland, right, one of many NIEHS researchers who made the trip to hear her seminar at Duke. (Photo courtesy of Steve McCaw)

To address this issue, Chan has worked to develop strains of zebrafish for mitochondrial studies. Zebrafish are extremely valuable for developmental research, Chan explained, because once fertilized, they rapidly develop and hatch within three days. Because they are transparent, her research group
(http://www.sherinechan.com/)
can use a microscope to watch embryonic development during exposure to different environmental toxicants. One toxicant the group has studied, rotenone, is a naturally occurring mitochondrial-targeting organic pesticide often used in farming.

Using zebrafish to determine mechanisms of birth defects and disease

The zebrafish model is particularly advantageous for Chan's research, because one of her interests is looking for connections between mitochondrial dysfunction and birth defects. Since many birth defects are sourced to the heart or nervous systems, which use a lot of mitochondrial-generated energy, Chan suspects that mitochondrial dysfunction could have a significant impact on early development.

Chan also detailed her study of epilepsy using zebrafish, and her search for an improved therapy using high-throughput zebrafish screens of potential compounds. Several promising compounds are being investigated by Chan's research group, in collaboration with MUSC chemist James Chou, Ph.D., and the National Institute of Neurological Disorders and Stroke Anticonvulsant Screening Program.
(http://www.ninds.nih.gov/research/asp/)
Their study was just accepted for publication in Neuroscience.

(Monica Frazier, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Mechanisms of Mutation Group.)

Transitioning from postdoc to lead researcher - building independence

In less than five years after leaving NIEHS, Chan and her group at MUSC have developed a new model system for studying mitochondrial disease, and successfully incorporated that system to establish new findings in the field.

Chan's former mentor, Bill Copeland, Ph.D., head of the NIEHS Mitochondrial DNA Replication Group and chief of the Laboratory of Molecular Genetics, is not surprised by her successful transition into an independent academic career.

"Her ability and tenacity to try new systems, such as working in the zebrafish model, something that she started on her own after leaving NIEHS and without any prior training, is especially impressive," said Copeland. Chan took advantage of a diverse range of training opportunities, while at NIEHS, and the effective transfer of those learned skills is a key component to her success.

"I was pretty open and not set on any one career path, so I explored many options, which is one of the many great things about doing a postdoctoral fellowship at the NIEHS," Chan commented. After becoming a recipient of an NIH Pathway to Independence (K99/R00) award from NIEHS, she was excited to follow an academic path.

The Environmental Factor is produced monthly by the National Institute of Environmental Health Sciences (NIEHS) *(http://www.niehs.nih.gov/)*
, Office of Communications and Public Liaison.

This page URL: NIEHS website: http://www.niehs.nih.gov/
Email the Web Manager at webmanager@niehs.nih.gov