

Investigator Spotlight: Qiang Chang, PhD, University of Wisconsin-Madison

As we enter the New Year, we are pleased to continue highlighting IRSF funded investigators in our Investigator Spotlight series. For the year's first installment, we are thrilled to feature Dr. Qiang Chang from the University of Wisconsin-Madison. Dr. Chang is an Assistant Professor in the Department of Medical Genetics and Neurology. His lab is focused on understanding the molecular mechanism of Rett syndrome and understanding the central role of MeCP2 in DNA methylation-dependent epigenetic regulation of brain development and function.



Dr. Chang received his PhD from the University of Pennsylvania in Neuroscience where he studied the development of motoneurons and neuromuscular junctions in mice in the lab of Dr. Rita Balice-Gordon. He also completed postdoctoral training in Dr. Rudolf Jaenisch's lab at the Whitehead Institute for Biomedical Research/MIT and studied the role of BDNF in RTT disease progression. Today, Dr. Chang's laboratory uses genetic engineering in mouse embryonic stem (mES) cells to manipulate the function of genes that play major roles in establishing and interpreting the epigenetic mark of DNA methylation in vivo, and integrates analyses at the molecular, cellular, electrophysiological, animal behavioral, and genomic levels to study these genetically engineered mice.

To complement their in vivo mouse models, his lab has recently generated isogenic pairs of induced pluripotent stem cell (iPSC) lines from a single female RTT patient carrying the common mutation R294X (5-6% of RTT patients have this mutation), and differentiated both the mutant and wild type iPSC lines into neurons and astrocytes. They are currently using this in vitro system to study RTT disease mechanisms and developing this as a platform for future drug screens. Dr. Chang was recently awarded a 2011 HeART translational grant to support these studies "Establishing Neurons Differentiated from an Isogenic Pair of Rett Syndrome iPSC lines as a Cell-Based Assay for Future Drug Screens".

Dr. Chang was also rewarded a 2008 basic research grant titled "Administering novel small molecules that have been shown to specifically activate TrkB in MeCP2 mutant mice to evaluate the therapeutic potential of BDNF". This work was recently published in the article "7,8-dihydroxyflavone (7,8-DHF) exhibits therapeutic efficacy in a mouse model of Rett syndrome" in the Journal of Applied Physiology. 7,8-DHF is a small molecule reported to activate the high affinity BDNF receptor (TrkB) in the central nervous system. The reported findings indicate the MeCP2 mutant mice that were treated with 7,8-DHF lived significantly longer, had delayed body weight loss, increased neuronal nuclei size, enhanced voluntary locomotor activity, and partially improved in breathing pattern irregularities compared to untreated mutant mice. While the specific mechanisms of 7,8-DHF are not completely known, it appears to reduce disease symptoms in MeCP2 mutant mice and may have potential as a therapeutic treatment for RTT patients.

What prompted you to begin a career in research?

I wanted to do something important and make a difference.

What is the single most rewarding aspect of conducting Rett syndrome research?

The hope that findings from my research will lead to a treatment/cure for Rett girls in the near future.

If you could pick any one symptom of Rett syndrome to prevent or to provide relief for, what would it be?

The growth and maturation of the neurons and the brain.

What other diseases does your research focus on?

My research program has a broad interest in neurodevelopmental disorders.

Besides your role as principal investigator on this project and as a Rett syndrome investigator, what other roles do you currently hold that are specific to the field of Rett syndrome research?

NIH grant reviewer, Autism Speaks grant reviewer, European Science Foundation reviewer, journal reviewer.

Provide any other interesting information about yourself or your work that you would like the Rett syndrome community to know about you.

I enjoy playing many sports. Away from science, I spend most of my time raising my two lovely children.

For more information on Dr. Chang, please visit:

www.waisman.wisc.edu/people/pi/Chang_Qiang.html.

For a list of Dr. Chang's publications, please visit:

www.ncbi.nlm.nih.gov.

For more information on the Rett Syndrome Clinic at Montefiore Medical Center, please visit:

www.einstein.yu.edu/neurology/program_details.aspx?id=100180

www.montekids.org/services/leadership/neurology/rett-syndrome/

www.eurekalert.org/pub_releases/2011-12/aeco-nen120111.php

7,8-dihydroxyflavone (7,8-DHF) exhibits therapeutic efficacy in a mouse model of Rett syndrome Johnson RA, Lam M, Punzo AM, Li H, Lin BR, Ye K, Mitchell GS, Chang Q.