IRSF Spotlight: Yi Eve Sun, PhD, University of California, Los Angeles

By Jim Keller

With this month's installment my goal to expose as many IRSF funded investigators who have a primary role in IRSF's 12th Annual Rett Syndrome Symposium to take place June 26th through 28th at the Lansdowne Resort and Spa in Leesburg, Virginia comes to a close. This month I saw fit to profile one of our meeting Chairs, Dr. Yi Eve Sun from the University of California, Los Angeles who is also a Co-Chair of this year's Session on animal and human cellular models of Rett syndrome (RTT) and is also a 2010 IRSF HeART Grant Award recipient. Her project titled "A high throughput small molecule screening platform for potential Rett Syndrome MBD mutation therapeutics" involves a search for candidate drugs that may enhance the binding of mutant MeCP2 protein to 'methylated' DNA. This work is important because RTT mutations frequently arise in the methyl-CpG binding domain (MBD) of the MECP2 gene. Such mutations of the gene are thought to result in the production of a misshapen MeCP2 protein that can no longer bind to methylated DNA. Dr. Sun's drug screen will be conducted using both biochemical test-tube based screens, in combination with cell-culture based screens (using stem cells with common RTT mutations). Taking this approach she hopes, may lead to the discovery of new drugs specifically targeted for individuals with RTT caused by MBD mutations.

Dr. Sun's early work was on the regulation gene expression and more specifically, focused on DNA transcription. DNA transcription is the main mechanism underlying many different events within biological systems in both health and disease. Commenting on her IRSF funded drug screen, Dr. Sun says *"Gene regulation has been the [consistent, but] ever changing theme in my studies from the outset of my career as an undergrad and Ph.D. student, a postdoctoral fellow, and now, as an independent principle investigator. This proposal is aimed at finding small molecules that may enable mutated MeCP2 to re-associate with methylated DNA."*

What prompted you to begin a career in research?
Curiosity! I grew up as a kid with enormous curiosity. I still remember the many nights in my childhood when I stood on our balcony staring at the starry night sky, wondering, with passion, what is out there? Then my imagination flew, freely, and far, far away. When I grew up, I thought of becoming an astrophysicist until I found another universe, even more mysterious, closer yet somehow further away, which sits inside but also connects outside our cranium, to the edge of the universe, the human mind. Like many people, I also wondered how the brain works, and that wonder has grabbed my attention ever since.

What is the single most rewarding aspect of conducting Rett syndrome research?
The hope and belief that we shall be able to help patients, a potentially solvable puzzle.

What is a potential positive outcome of the research you're conducting that is specific to your IRSF Award?
We might be able to find drugs that will be specifically used to enable particular mutant MeCP2 to regain its

ability to bind DNA, and therefore restore normal MeCP2 function. Since these mutations result in changes to only a single amino acid, it is possible that it could be a relatively simple problem to "fix" by essentially going around them.

If you could pick any one symptom of Rett syndrome to prevent or to provide relief for, what would it be?
There are many candidate drugs I can think of, however, to be able to enable mutant MeCP2 to re-associate with methylated DNA essentially gets to the root of the problem. While it will not work with all kinds of MeCP2 mutations, even if only a subset of patients with particular mutations can be treated, it will be enormously rewarding.

What other diseases does your research focus on?
Parkinson's disease, spinal cord injury, and other autism-spectrum disorders.

What else would you like the RTT community to know about you?
I am a chartered reviewer for NIH, and I review many RTT-related grants. I also sit on IRSF's Scientific Review Board, and review for many journals on RTT research-related manuscripts.

I like to explore the power and the biology of the human unconscious mind. I am a certified hypno – therapist—though admittedly, I need more time to practice, and I'm currently learning how to ballroom dance. I was once a semi-professional swimmer and springboard-diver as well.

Please visit this page to register for the Symposium and to view a list of confirmed speakers.