

John M. Bissonnette, MD of Oregon Health and Science University

October 11, 2010

By Jim Keller

Note: The IRSF Spotlight's intent is to give our lay and scientific communities an idea of who IRSF funded investigators are both as a person and a scientist working to make Research a Reality.

Last week IRSF reported on a study published in the journal, Proceedings of the National Academy of Sciences, which focused on how a team of researchers based in the U.S. and UK revealed that they were able to halt the potentially lethal, breath holding episodes associated with Rett syndrome. These investigators were none other than Dr. John M. Bissonnette and his collaborator Dr. Julian FR Paton of the University of Bristol, co-Principal Investigators (co-PIs) on the recently announced IRSF Research Grant, titled "Pharmacological treatment of respiratory disorders in a mouse model of Rett syndrome." In addition, Dr. Bissonnette was also the recipient of one of the first IRSF Help Accelerate Rett Therapeutics (HeART) Awards, titled "Serotonin and small molecule treatment of respiratory disorders in a mouse model of Rett syndrome," and is a member of IRSF's Scientific Review Board (SRB). With his numerous contributions to the Rett community, we thought it was time to introduce Dr. Bissonnette who was kind enough to answer a few questions on the eve of Rett syndrome Awareness Month.

Dr. Bissonnette studied medicine at McGill University in Montreal, Canada, during which he spent a month in a basic research lab as a first year student. He was assigned to a group working on encephalitis, which served as his introduction to the central nervous system. As a resident he again had basic research exposure examining acid-base regulation in rhesus monkey fetuses. Following a post-residency fellowship, Dr. Bissonnette established a laboratory that studied control of respiration in fetal sheep until 1997, when the lab redirected to work with mice to take advantage of mouse genetics. RTT mice are unique in that they have a high incidence of spontaneous apneas and may lead to a greater understanding of a broad range of respiratory control disorders.

What prompted you to begin a career in research?

After I had finished my clinical training I was a post-doctoral fellow in a cardiorespiratory physiology laboratory. I became captivated by the process of moving from experimental data to concepts of "how things work" and that process remains after many years.

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

For the first time in my research career I am working on an animal model of a human disorder.

What is a potential positive outcome of the research you are conducting that is specific to your latest IRSF Awards?

There are two arms to our current program. In one, we are attempting to identify the location within the respiratory network (that has a number of centers distributed within the pons, medulla and cervical spinal cord) where excess activity of expiratory neurons reside. At present, we are focused on the Kölliker-Fuse nucleus in the pons. We are looking at the inhibitory synapses that attach to Kölliker-Fuse neurons.

The second arm of our research may lead to treatment of respiratory disorders in RTT. We recently found that serotonin 1a receptor agonists markedly reduce apnea in RTT mice and restore regularity to their breath cycle. The pharmacological agent used, however, is not clinically available. We are now testing an alternate serotonin 1a agonist, Sarizotan. Sarizotan has been used in phase 2 human trials to treat levo-dopa-induced dyskinesia in Parkinson's disease. If successful it could advance to clinical testing more rapidly than an untried drug.

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

From my limited clinical observations I would look for relief of the purposeless body movements.

What other disease(s) does your research focus on?

RTT is the only mouse model that we are studying, but an understanding of the basis for respiratory disturbances in RTT may have wider implications.

What else would you like the RTT community to know about you?

When not in the lab I enjoy hiking in the many mountain areas available in Oregon. Weather permitting, I bicycle to the lab. At home I enjoy cooking and walking our Labrador-mastiff mix dog. Also, I have been privileged to have Sharon Knopp as my laboratory associate for over 25 years.