Genetics 101 An update September 7, 2010

There have been several key developments in our understanding of the role of other specific genes that are involved in causing an arrest in the development of immature nerve cells that we call Rett Syndrome (RS).The three genes in particular are Fox G1, CDKL 5 and MeCP2. The mutations in the first two cause the atypical, early onset form of RS while mutations in MeCP2 are responsible for the classic form. A forth gene, BDNF is of great interest because it is a key player in the process of developing connections between nerve cells. Fox G1 CDKL5, MeCP2 and BDNF are working in a sequence of activities involved in the process of developing these connections .This sequence is termed a signaling pathway.

At key chemical in the brain is termed GABA that plays an inhibitory role in regulating signaling pathways. Most recently researchers working with Dr. Huda Zhogbi have developed a method to "knock out" the gene MeCP2 in brain cells which make GABA. As a consequence the animal model developed many of the signs and symptoms of RS. This group goes on to suggest that a disruption in this pathway is responsible not only for RS but several neurodevelopment disorders including cognitive disorders, autism, as well as juvenile-onset schizophrenia. These findings will likely serve to recruit additional investigators from other neuroscience laboratories which can only help to speed up our understanding of RS. Currently there are a number of drugs on the market which can increase the levels of GABA within the brain. This comes at a time when there is talk of expanding clinical trials targeting that three common problems experienced by RS patients. These are the abnormal breathing patterns, chronic constipation and seizures. However a major problem in establishing any clinical trial is having access to a meaningful number of cases to enroll, a minimum number would be 100. To address this the Rett Syndrome Research Foundation together with a group of European investigators are planning to develop an international registry of RS patients and from this, develop a research a registry of interested families.

The Retts Canada consortium is focused on developing a national team of basic scientists and clinical investigators to target these three co-morbidities. We are preparing to submit another letter of intent to the Canadian Health Research Institute on January 1, 2011. Part of the funding request includes a proposal to establish a Canadian registry along the lines of the international registry so that we can begin a series of projects in the run-up to clinical trials. A busy time for all! Stay tuned….

Patrick Macleod.