Understanding the MECP2 gene

There is still much to be learned about the function of the MECP2 gene. It is a very important gene and acts as a regulatory gene for thousands of other genes. MECP2 can cause both increased expression and decreased expression of other genes at critical times in development. The MECP2 gene plays a critical role in brain development and brain function.

The MECP2 gene is located on the X chromosome, one of the sex chromosomes. Females typically have two X chromosomes and males typically have one X chromosome and one Y chromosome. Thus, all females typically have two copies of the MECP2 gene, one on each of their X chromosomes. Females with Rett syndrome have a mutation or a change in one copy of the MECP2 gene on one of their two X chromosomes. Because of a process known as X inactivation, only one copy of the MECP2 gene is active in any one cell in females. This X inactivation process is random, so that in some cells the MECP2 gene with the mutation is active and in other cells the MECP2 gene without the mutation is active. In females with Rett syndrome this means that roughly half of their cells have a normally functioning MECP2 gene and half their cells have a MECP2 gene with a mutation present that is not functioning normally. This is the typical pattern seen in Rett syndrome.

Males only have one X chromosome and, only one MECP2 gene. Thus, a male with a mutation in the MECP2 gene has that mutation present in their only copy of the MECP2 gene. Therefore, the function of MECP2 is affected adversely in all cells in the male. This is why males with MECP2 mutations present differently than females with MECP2 mutations. Males that have a mutation that is similar to the typical mutation seen in females with Rett syndrome present with early onset and more severe clinical problems than females with classic Rett syndrome.

Early on it was felt that males with MECP2 mutations were nonviable, thus, explaining the absence of the diagnosis of Rett syndrome in males. However, it was subsequently determined that most of the mutations in MECP2 are due to new spontaneous mutations in the MECP2 gene that occur during the division and formation of sperm, the male germ cell. Since fathers typically give their X chromosome to their daughters and their Y chromosome to their sons, this explains the low occurrence of males with MECP2 mutations.