Genetics of Fragile X Syndrome

Fragile X syndrome arises from a genetic mutation to a gene on the X chromosome. It is this mutation that causes a section of the lower half of the X chromosome to appear ‘fragile,' providing the origin of the syndrome’s name.

In particular, it is the FMR1 gene on the X chromosome that is affected in fragile X syndrome. Mutation of this gene is the most common mechanism of genetic abnormality. However, a few individuals may have a deletion of the FMR1 gene or have a different genetic make-up (mosaicism) of the gene.

The FMR1 gene is partly made up of a cytosine, guanine and guanine (CGG) DNA pattern which repeats a variable number of times, and this is known as a trinucleotide repeat. In typically developing individuals the number of trinucleotide repeats ranges from 1 to 55 times. However, in individuals with full mutation fragile X syndrome the CGG sequence is repeated over 200 times causing the gene to be turned off. If the number of repeats is between 55 and 200, the individual is said to have premutation fragile X syndrome.

The FMR1 gene produces FMR protein (FMRP); however the mutation of the gene in fragile X syndrome means that there is a decrease in the production of FMRP. The role of FMRP is still not fully understood, but it is thought to be associated with the development of the brain, in particular, the way that connections in the brain are regulated, such as getting rid of weaker connections (synaptic pruning).

Further information:

A good resource for the genetics of fragile X can be found here.

The Fragile X Society have also posted a video on the Genetics and Diagnosis of Fragile X Syndrome which can be found on their website:

http://www.fragilex.org.uk/testing