Is mental retardation heritable?

Mental retardation, or intellectual disability, refers to persistently poor memory, weak cognitive, comprehension and problem-solving skills during childhood; and below-normal global intellectual capacity during adulthood. It affects 3 out of every 100 individuals. These individuals have an intelligence quotient (IQ) below 70. Mental retardation is caused by a number of different factors. Among genetic disorders, Fragile X syndrome and Down syndrome are the commonest causes of mental retardation.

Fragile X syndrome (FXS) is an inherited form of mental retardation. FXS is estimated to affect 1 in 2,500 males and 1 in 8,000 females. This syndrome is caused by a mutation in the *FMR1* gene which in turn affects the normal production of FMRP protein. Within the *FMR1* gene there is a stretch of CGG trinucleotide repeats of variable length. Normal people have 6-54 CGG repeats in this region. However, people with FXS have abnormal expansion of the CGG trinucleotide repeats to over 200 times. This is called full mutation and affected patients have characteristic craniofacial features (including large head and ears, long face, thickening of nasal bridge and prognathism). Patients have variable intellectual problems, including mental retardation, hand flapping or biting behaviour, lack of eye contact and cluttering or repetitive speech. Affected females have milder symptoms as compared to males. The family members of affected individuals may have 55 to 200 CGG repeats in this region and are said to have a premutation. Premutation carriers do not have FXS but some of them may have other manifestations, including premature menopause (before 40 years of age) in women and neurological disorder (presenting with unsteady gait and intention tremor, especially in males) after 50 years of age.

FXS is inherited in an X-linked dominant manner. Males inheriting the full mutation from their mothers will develop symptoms while females inheriting the full mutation also have about 50% chance being affected. Affected males will not pass the mutant gene to his sons but all his daughters will be premutation carriers. On the other hand, each offspring of a female carrier will have 50% of inheriting the mutant gene. For prevention, female carriers can undergo amniocentesis during pregnancy to ascertain the sex of the fetus and whether or not the mutation was inherited.

Clinical Genetic Service
Department of Health
(2012 Version)