Measuring intellectual disability

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Researchers from the University of California, Davis have developed a specific and quantitative means of measuring levels of the fragile X mental retardation 1 (FMR1) protein (FMRP), which is mutated in fragile X syndrome. The related report by Iwahashi et al, "A quantitative ELISA assay for the fragile X mental retardation 1 protein," appears in the July 2009 issue of the *Journal of Molecular Diagnostics*.

Fragile X syndrome is the most common form of inherited intellectual impairment. Nearly one third of patients diagnosed with fragile X syndrome also have some degree of autism, and the mutation underlying fragile X syndrome is the most commonly known single gene cause of autism.

Fragile X syndrome is caused by low levels of the FMRP protein, which is thought to play a role in communication between nerve cells. In patients with fragile X syndrome, a sequence in the FMR1 gene that is repeated 10-40 times in normal individuals may be repeated from 200 to more than 1,000 times, decreasing levels of the FMRP protein.

Current tests for fragile X syndrome determine the presence of the mutation by measuring the number of repeats at the DNA and mRNA level; however, the lack of a quantifiable test to determine FMRP protein levels has prevented direct correlation between FMRP protein levels and clinical severity of disease. Therefore, a group led by Dr. Paul Hagerman at the University of California, Davis developed a sensitive and highly specific test for FMRP protein. The method used is able to detect protein throughout the biologically-relevant range of protein

concentrations and is readily adaptable for large-scale use.

Iwahashi et al suggest that "[this] method should prove to be a powerful tool for further investigation of the relationships between FMRP and the diverse clinical phenotypic domains [of fragile X syndrome]." "Such domains include not only autism and autism spectrum disorders, but also developmental delay, behavioral difficulties, anxiety, ADHD, and mood. Involvement among carriers of smaller (premutation) alleles can also involve developmental delays and/or autism spectrum disorders." In future studies, Dr. Hagerman and colleagues plan to explore "further large scale studies … to recognize the value of the measurement and how FMRP influences the multitude of phenotypes associated with the FMR1 gene and variations seen in the normal population."

More information: Iwahashi C, Tassone F, Hagerman RJ, Yasui D, Parrott G, Nguyen D, Mayeur G, Hagerman PJ: A quantitative ELISA assay for the fragile X mental retardation 1 protein. *J Mol Diagn* 2009, 281-289

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