

Stephanie L. Sherman, Ph.D.

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Biographical Information

Stephanie L. Sherman obtained her Ph.D. in Human Genetics from Indiana University School of Medicine in 1981 and is currently a Professor in the Department of Human Genetics at Emory University in Atlanta, GA. Her training is in the area of genetic epidemiology and she has been involved in coordination of multi-site projects to ascertain families to unravel the genetic architecture of complex traits and to understand potential gene-environment interactions. Dr. Sherman's research program focuses on the identifying the neuropsychological, neurological and co-occurring conditions among individuals who carry the *FMRI* premutation. Among women, this includes identifying factors that increase the risk for fragile X-associated primary ovarian failure (FXPOI) and, among men, those that are involved in fragile X-associated tremor/ataxia syndrome (FXTAS).

Presentation Abstract (4:30 pm presentation)

Fragile X-associated Disorders: A Woman's View from the Heart of the Family

Fragile X syndrome is the most common inherited form of intellectual and development disabilities that is often accompanied by significant behavioral problems. It is due to a dynamic repeat sequence mutation in the X-linked *FMRI* gene that occurs in about 1/4000 males and 1/8000 females. All mothers of children with FXS carry the *FMRI* mutation in some form, most often the "premutation" form. Although the premutation allele seldom leads to developmental disorders, we now know that it increases the risk for at least three clinically significant manifestations among women. First, during transmission from parent to child, this allele can expand to the full mutation, or the form that leads to FXS in offspring. This expansion only occurs during transmission of the mutation from mother to child, not from father to child. Second, the premutation leads to an increased risk for fragile X-associated primary ovarian insufficiency (FXPOI), a disorder that can lead to subfertility and to other clinical consequences associated with early estrogen deficiency. Third, the premutation is associated with fragile X-associated tremor/ataxia syndrome (FXTAS), a neurodegenerative disorder that is more common in men who carry the premutation, but also occurs in a significant number of women. There are other possible manifestations of the premutation, possibly exacerbated by genetic and environmental factors, which are just now being realized. Women with the premutation play a central role in the lives of their family members, commonly caring for a child and parent with fragile X related disabilities — this role demands their good health and well-being. In this presentation, I will review the clinical consequences of the premutation among women and emphasize the need for further study and identification of interventions to ensure that women who are at the heart of families with fragile X-associated disorders can themselves have full and healthy lives and, at the same time, facilitate those qualities for her family members.