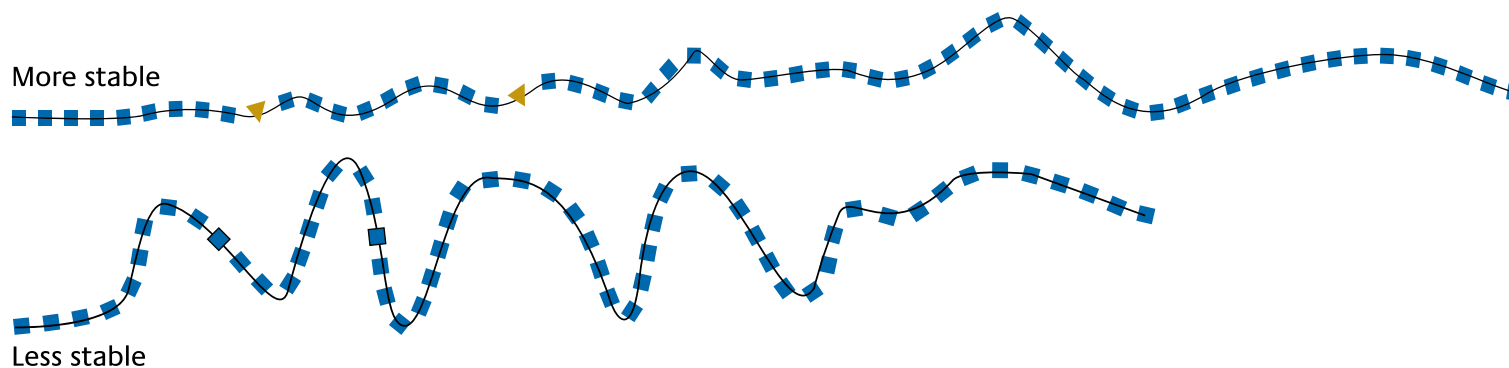


Different Forms of the Fragile X Gene

Name	CGG Repeat Sizes	Common Features	CGG Stability
Normal	<45	No features or syndrome are present	Stable
Intermediate	45-55	No features or syndrome are present	Uncertain stability
Premutation	55-200	Some individuals develop movement problems over approximate age of 55; Some women have infertility and/or early menopause	Unstable
Full mutation	>200	Features of Fragile X syndrome in males and some females	Unstable

AGG Interruptions Stabilize the Fragile X Gene



Fragile X Testing Summary

- The number of CGG repeats in the Fragile X gene determines the chances that a person will have features of Fragile X syndrome or related disorders.
- The number of CGG repeats also influences whether those CGG repeats will remain stable or change (expand) when being passed to a person's child.
- AGG interruptions within the CGG repeat region help stabilize it, making it less likely to expand when it is being passed down to a person's child.

AGG interruptions within the 5' UTR CGG repeats of the Fragile X *FMR1* gene have long been suggested to stabilize alleles to protect against expansion (Eichler 1994; Kunst 1994; Zhong 1996; Nolin 1996). However, technological challenges prevented the clinical evaluation of the relationship between AGG interruptions and the probability for expansion.

A large, multi-center study examined CGG repeats and AGG interruptions in 456 mother-to-child transmissions for carriers of alleles with 45-69 total repeats. The study showed a clear modification of the probability of expansion, of variable sizes and degrees, when the number and location of AGG interruptions and uninterrupted CGG repeats were considered.

Figure 1: Probability and magnitude of expansion in 456 mother-to-child transmissions based on the number of uninterrupted 3' CGG repeats within the 5' UTR of *FMR1*.

Figure 2: Modification of expansion risk based on measuring both CGG and number of AGG interruptions.

Figure 1

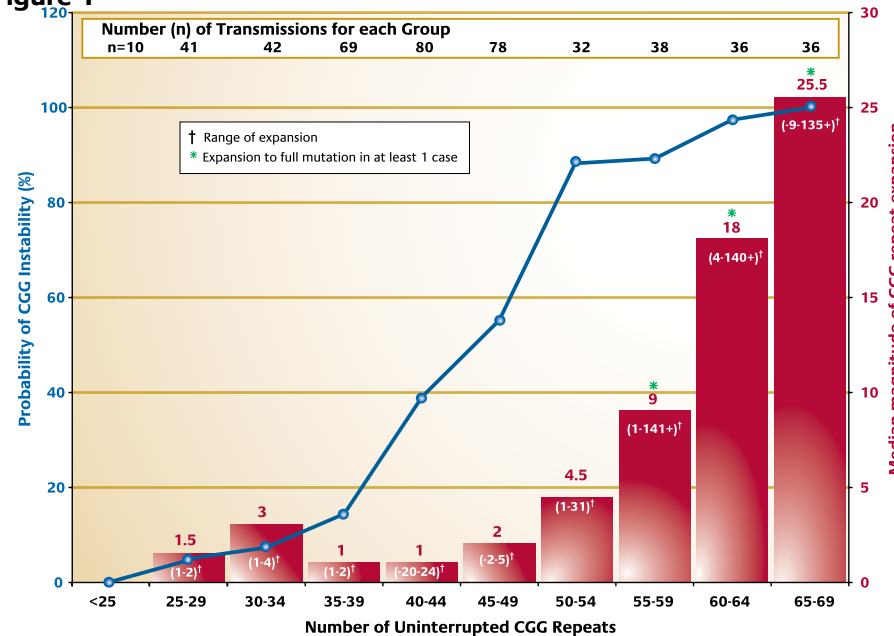
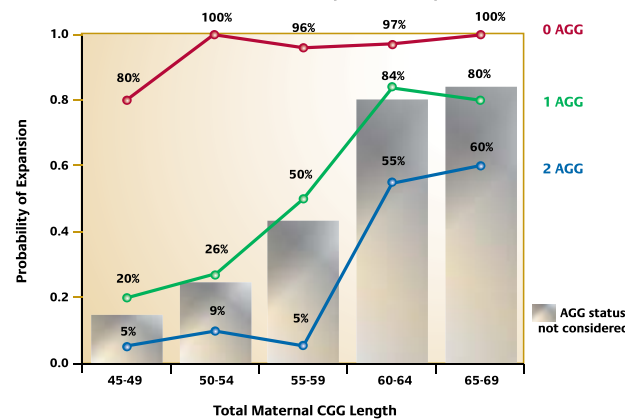


Figure 2



AGG Genotyping

Appropriate to offer women with*:

- Fragile X repeat results in the 45-69 total CGG repeat range

and who are

- Considering pregnancy, are pregnant, or seeking fertility treatment

*Data supporting these recommendations were presented at multiple scientific conferences such as:

- International Workshop on Fragile X, 2011
- ICHG/ASHG, 2011
- American College of Medical Genetics, 2011