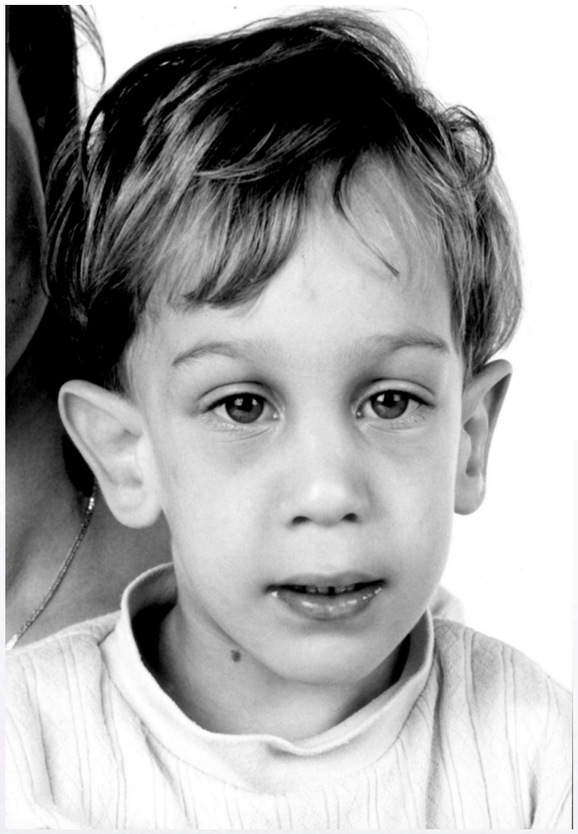
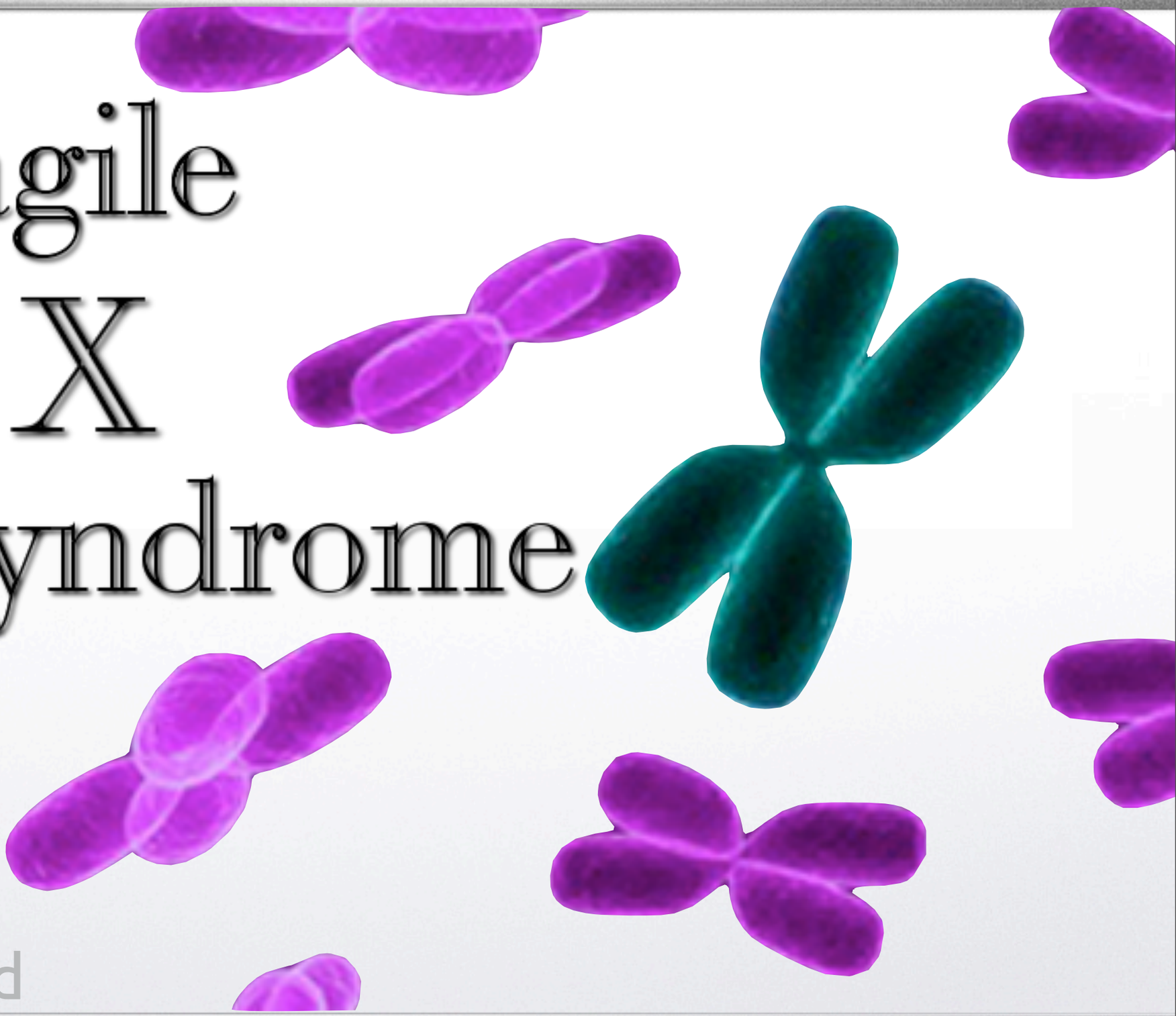
Fragile X Syndrome



Source: http://jmg.bmj.com



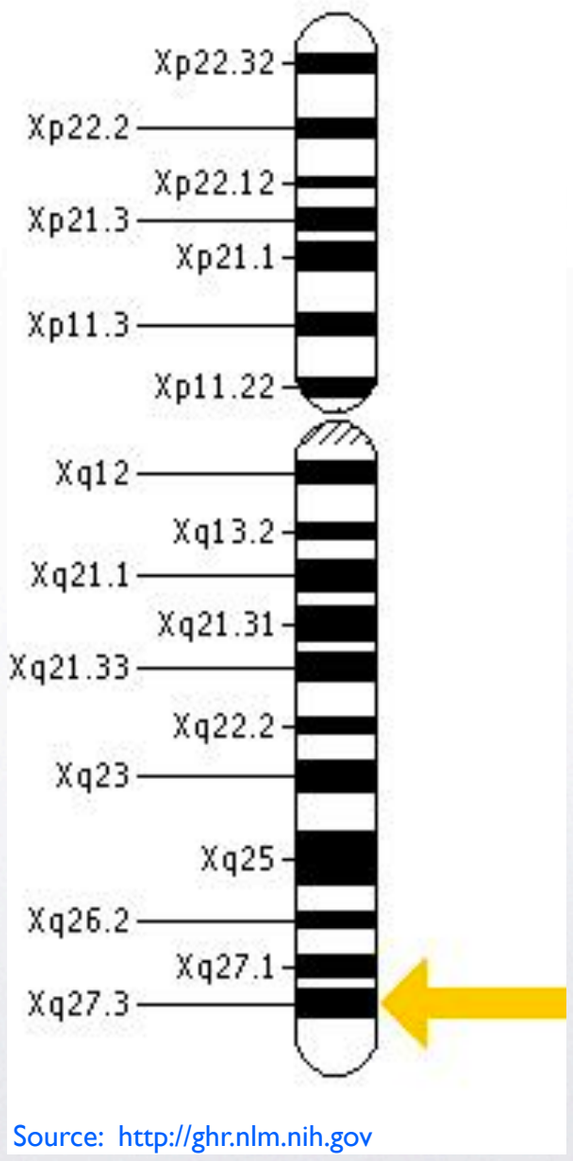
by Marie Hubbard

Background

- Most common form of inherited intellectual disability in boys
- Characteristic appearance in boys: long face, protruding ears, broad forehead, low muscle tone
- Behavioral abnormalities: developmental disabilities, autism spectrum disorder
- An FMR1 mutation is responsible for about 5% of autism cases

Underlying Genetics

- FXS is caused by a loss-of-function mutation in the FMR1 gene on the X chromosome
  - ➔CGG trinucleotide repeat expansion and abnormal gene methylation



Source: http://ghr.nlm.nih.gov

- Affected Gene

  Official Name: “Fragile X Mental Retardation 1”

  Gene Symbol: FMR1

  Locus: Xq27.3

Diagnostic Methods

- Classical

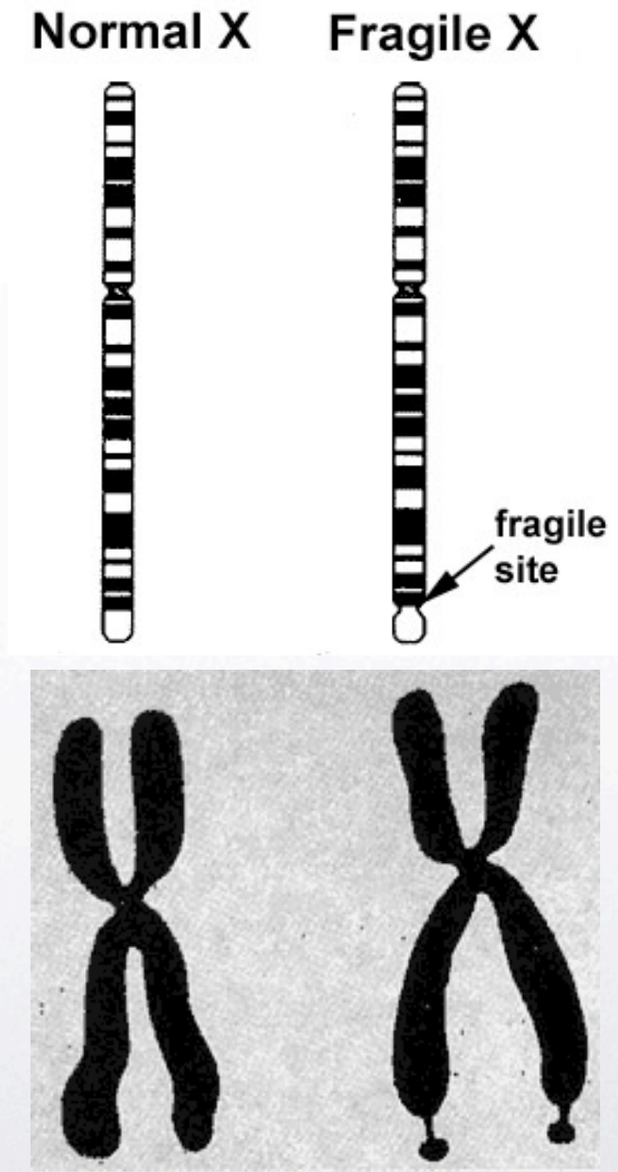
  IQ tests, behavior observation

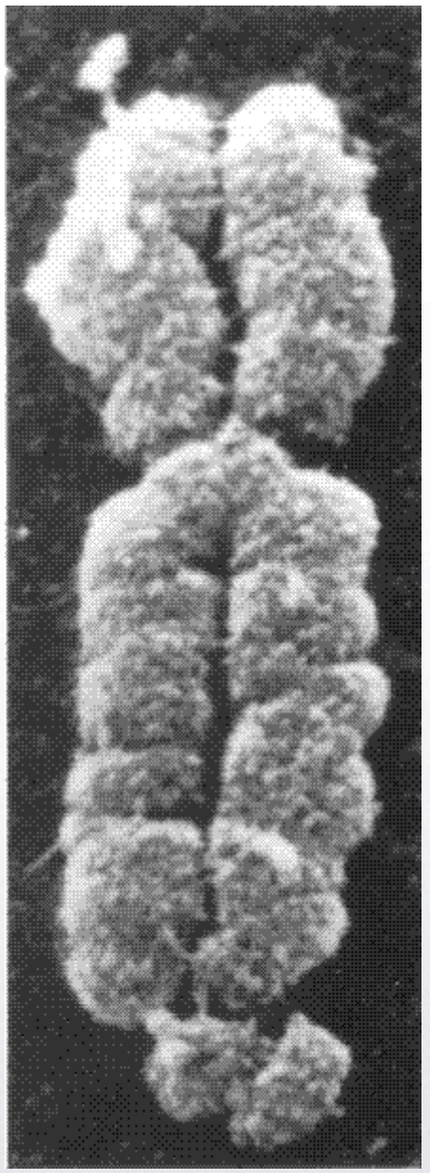
- Novel

  ➔Cytogenetics

  ➔Protein Testing

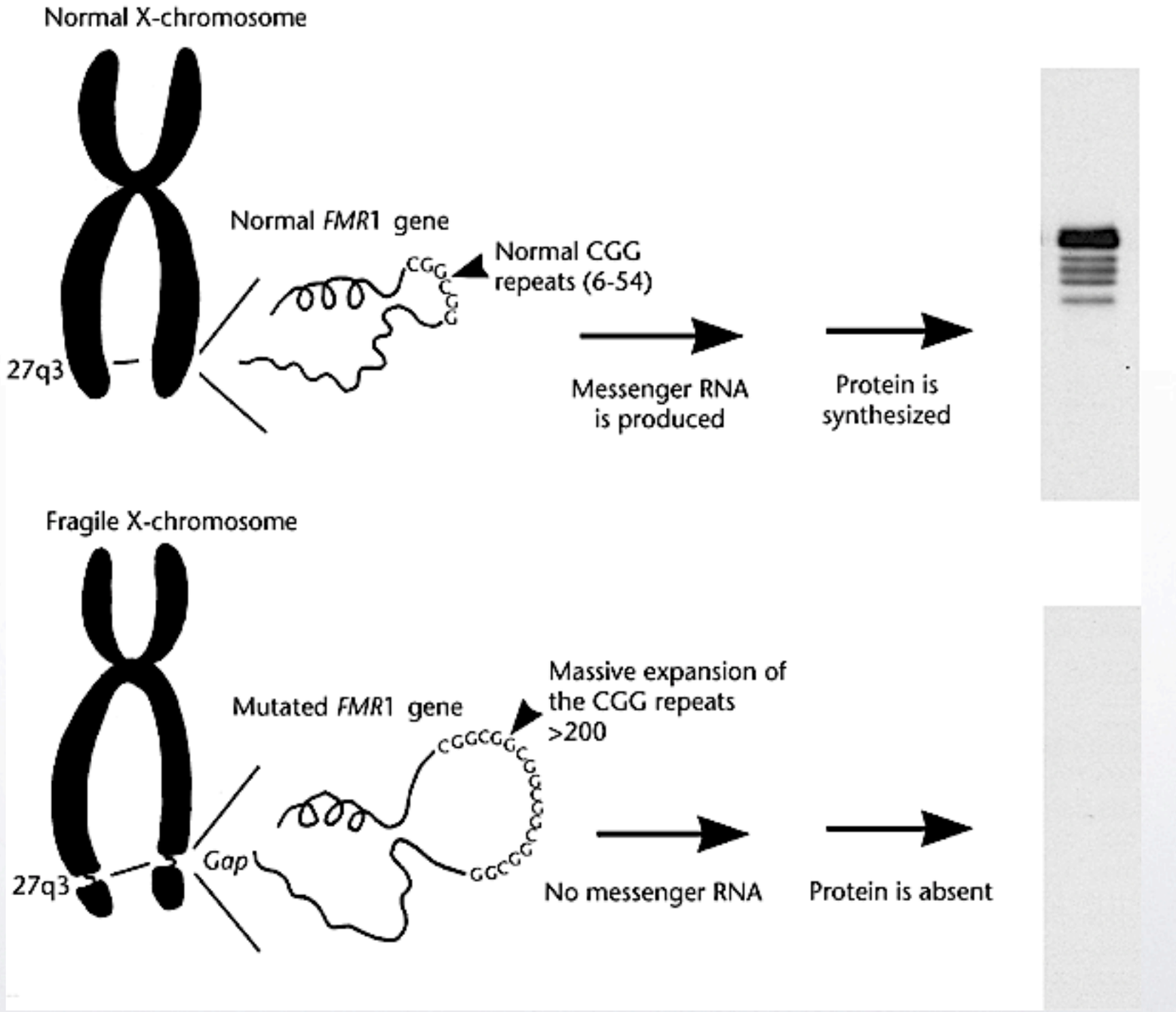
  ➔Molecular Genetic Testing





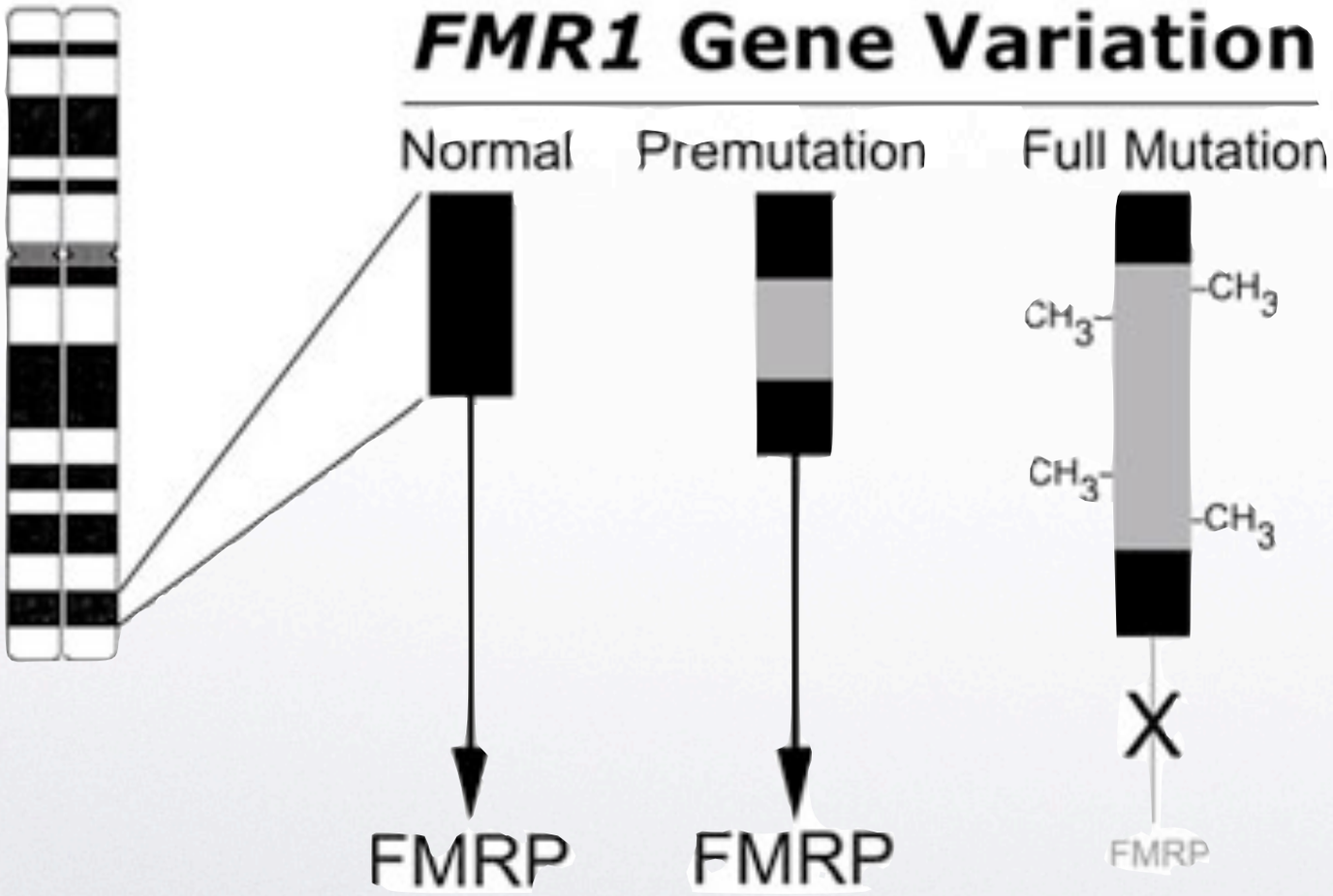
Protein Testing

- FMR1 protein (FMRP) is not produced in individuals with FXS
- Some labs will measure the production of FMRP to diagnose FXS



Source: http://www.els.net/

Molecular Genetic (DNA) Testing



Source: http://cibsr.stanford.edu

- Severity of FXS is correlated with the number of CGG repeats
- Number of repeats

  Normal Alleles: 5-44

  Premutation: 55-200

  Mutation (FXS): more than 200
- Best diagnostic method

Treatment Methods

- Genetic understanding has not led to a novel treatment
- Early intervention, special education
- Pharmacological treatment for specific symptoms (i.e. ADHD medication, anxiety medication)

Sources

- http://www.ncbi.nlm.nih.gov
- http://ghr.nlm.nih.gov
- http://www.sciencedirect.com