Fragile X Syndrome

- Most common form of inherited form of mental retardation
- 1/3600 males, 1/4000-6000 females
- IQ 40-70
- Delayed developmental milestones
- Connective tissue problems
- ADD, autistic behaviors, unusual responses to stimuli
- Epilepsy
- Associated with FMR1 gene
- X-Linked Dominant
- Gene Map Location: Xq27.3
- Greater than 200 CGG repeats, FMR1 gene is not expressed
  - Loss of function
- Normal individuals: 60 repeats
- Premutation: 60-200
- FMRP works with polyribosomes and their particles
  - FMRP protein needed for RNA binding
  - Transcriptional suppression in 95% of cases
- Also associates with 800 brain mRNAs
- Mechanism not fully understood
Males with more than 200 CGG repeats = mentally retarded and do not reproduce.

Females with more than 200 CGG repeats may not be mentally retarded.

Unaffected X chromosome may produce enough FMRP protein.

Premutation levels sometimes express the mutation:

- Fragile X-associated tremor/ataxia syndrome (FXTAS)

- Late-onset progressive cerebellar ataxia and intention tremor.
In the 70’s and 80’s:
- Chromosomal testing
  - Not always accurate
- Protein testing to measure the production of FMR1 protein
In 1990, 2 molecular DNA tests became available.

- **Southern Blot analysis**: cuts DNA into pieces, attaches radioactive probes to analyze specific areas.
- **Polymerase Chain Reaction (PCR)**: makes millions of copies of the FMR1 gene for analysis.

Both methods can diagnose Fragile X and detect carriers.

- Most accurate when both tests are used.
- The National Fragile X Foundation suggests genetic testing for any female thinking of having children with fragile X in the family or a relative of undiagnosed mental retardation.

- 1 in 300 females are carriers.
- No cure for Fragile X, but:
  - Special Education
  - Speech therapy
  - Occupational/behavioral therapy
  - Medication for symptoms like hyperactivity of ADD

http://www.youtube.com/watch?v=_byqoPW_XFk&feature=related
Deficit in synapse elimination in Fragile X Syndrome?

- New research on Tandem Repeat Polymorphisms
  - Source of genetic variability (like SNPs)

-clinicaltrials.gov
Works Cited

First image:
http://www.google.com/imgres?um=1&hl=en&sa=N&biw=1366&bih=653&tbm=isch&tbnid=BReSkIrah32bIM:&imgrefurl=http://medgen.genetics.utah.edu/fragilex/facts.html&w=284&h=326&ei=IWITT7agB8GviAKm2Ny0DQ&zoom=1

Second image:

Third Image:
http://www.google.com/imgres?um=1&hl=en&sa=N&biw=1366&bih=653&tbm=isch&tbnid=Ts1WJuxf0bIkBM:&imgrefurl=http://ocw.tufts.edu/Content.html&docid=Q&zoom=1&iact=rc&dur=413&sig=116918143262329443334&page=1&tbnh=125&tbnw=167&start=0&ndsp=24&ved=1t:429,r:6,s:0&tx=98&ty=40

http://www.ncbi.nlm.nih.gov/books/NBK22189/

Chromosome Picture:

http://www.subtelomeres.com/ClinicalDiagnosis_6.html

Tim Tran paper: Fourth Image

http://www.fragilex.org/html/diagnosis.htm

Fifth image:

Kimberly Huber slides

Image of child in school: