FRAGILE X SYNDROME

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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

The 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

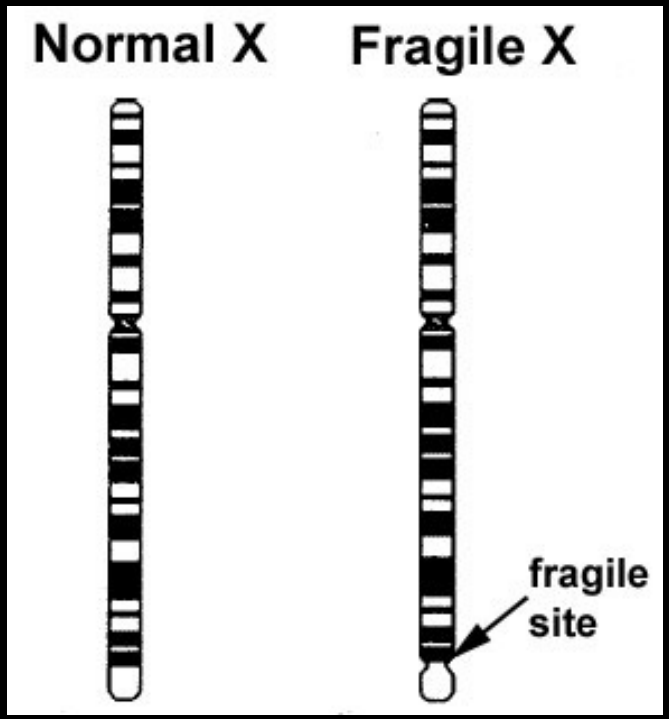
-FMRP works with polyribosomes and their particles

-FMRP protein needed for RNA binding

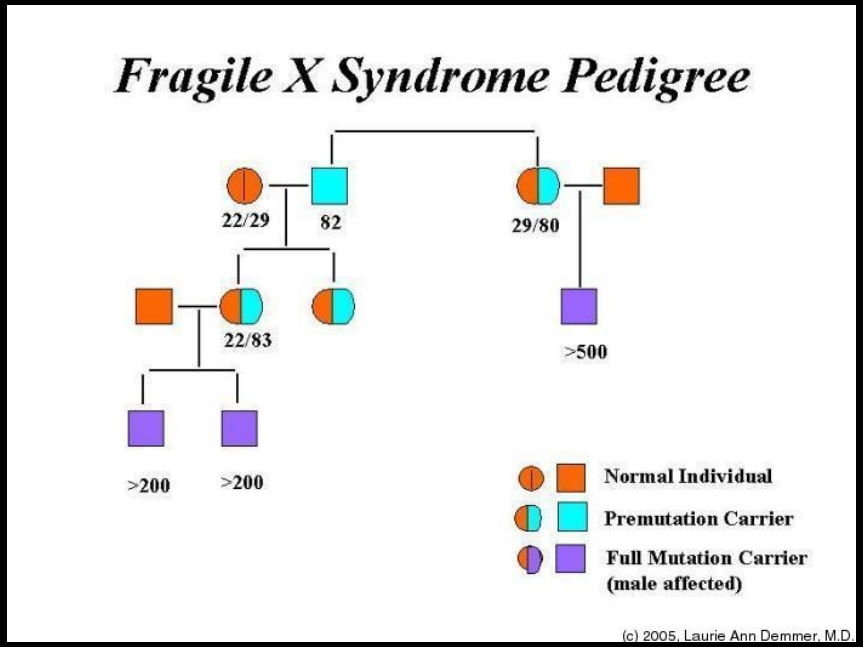
-Transcriptional suppression in 95% of cases

-Also associates with 800 brain mRNAs

-Mechanism not fully understood



Penetrance



-Males with more than 200 CGG repeats=mentally retarded and do no reproduce

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

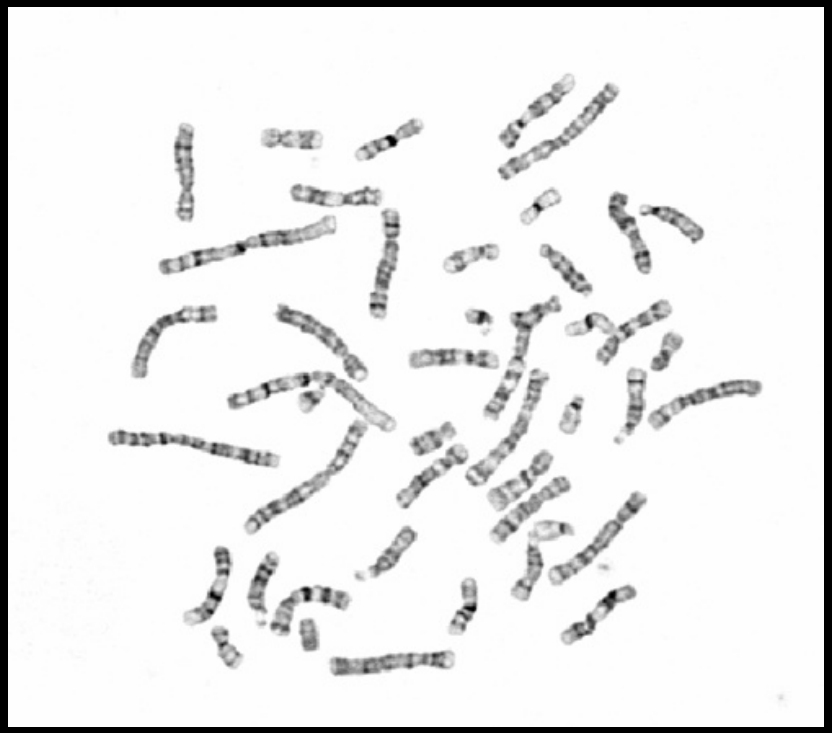
-Unaffected X chromosome may produce enough FMRP protein

-Premutation levels sometimes express the mutation:

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

-Late-onset progressive cerebellar ataxia and intention tremor

Classical Diagnosis



-In the 70's and 80's: chromosomal testing

-Not always accurate

-Protein testing to measure the production of FMR1 protein

Novel Diagnostics

-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

Treatment

-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

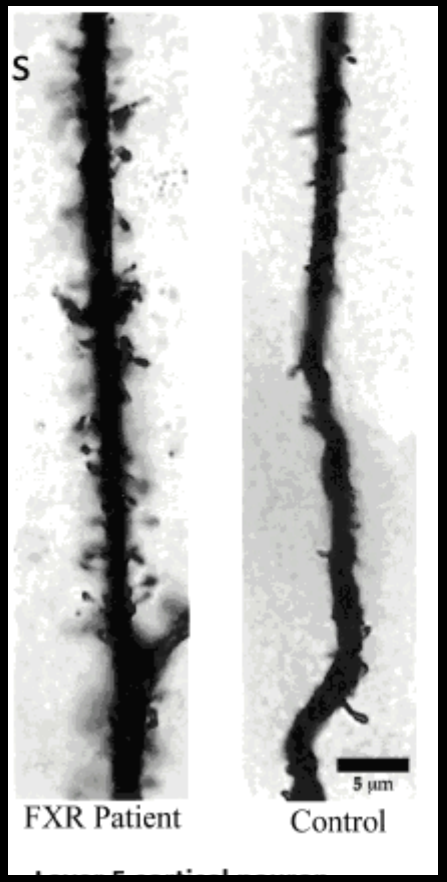
Future?

-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

Second image:
http://www.google.com/imgres?um=1&hl=en&sa=N&biw=1366&bih=653&tbm=isch&tbnid=lMoTBqnl9mLZSM:&imgrefurl=http://thefertilityblogs.co
thefertilityblogs.com/files/2010/07/Fragile-X.jpg&w=293&h=316&ei=AEETT4yoA4iYiALm1_SrDQ&zoom=1&iact=hc&vpx=401&vpy=163&dur=234

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/Conter

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

http://ghr.nlm.nih.gov/condition/fragile-x-syndrome

Works Cited Continued

Chromosome Picture:

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

Tim Tran paper: Fourth Image

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

Fifteh image:
http://www.google.com/imgres?um=1&hl=en&biw=1366&bih=653&tbm=isch&tbnid=omezZ3ItROkmxM:&imgrefurl=http://www.ic-mp.org/facililities

Kimberly Huber slides

Image of child in school:

http://www.google.com/imgres?num=10&hl=en&gbv=2&biw=1366&bih=653&tbm=isch&tbnid=4swCWBQ8NvrDxM:&imgrefurl=http://www.buzzle.com/articles/interesting-facts-about-fragile-x-syndrome.html&docid=ZiXXW07hxtSoSM&imgurl=http://www.buzzle.com/img/articleImages/272 174-44827-24.jpg&w=350&h=233&ei=dewc1-eiFpSOgLfg8XGCA&zoom=1&iact=rc&dur=370&sig=116918143262329443334&sqi=2&page=1&tbnh=118&tbnw=178&start=0&ndsp=24&ved=1t:429,r:22,s:0&tx=110&ty=29