Dr. Nedwidek/ Stuyvesant High School
Michelle Chen
SBS11QHG-02
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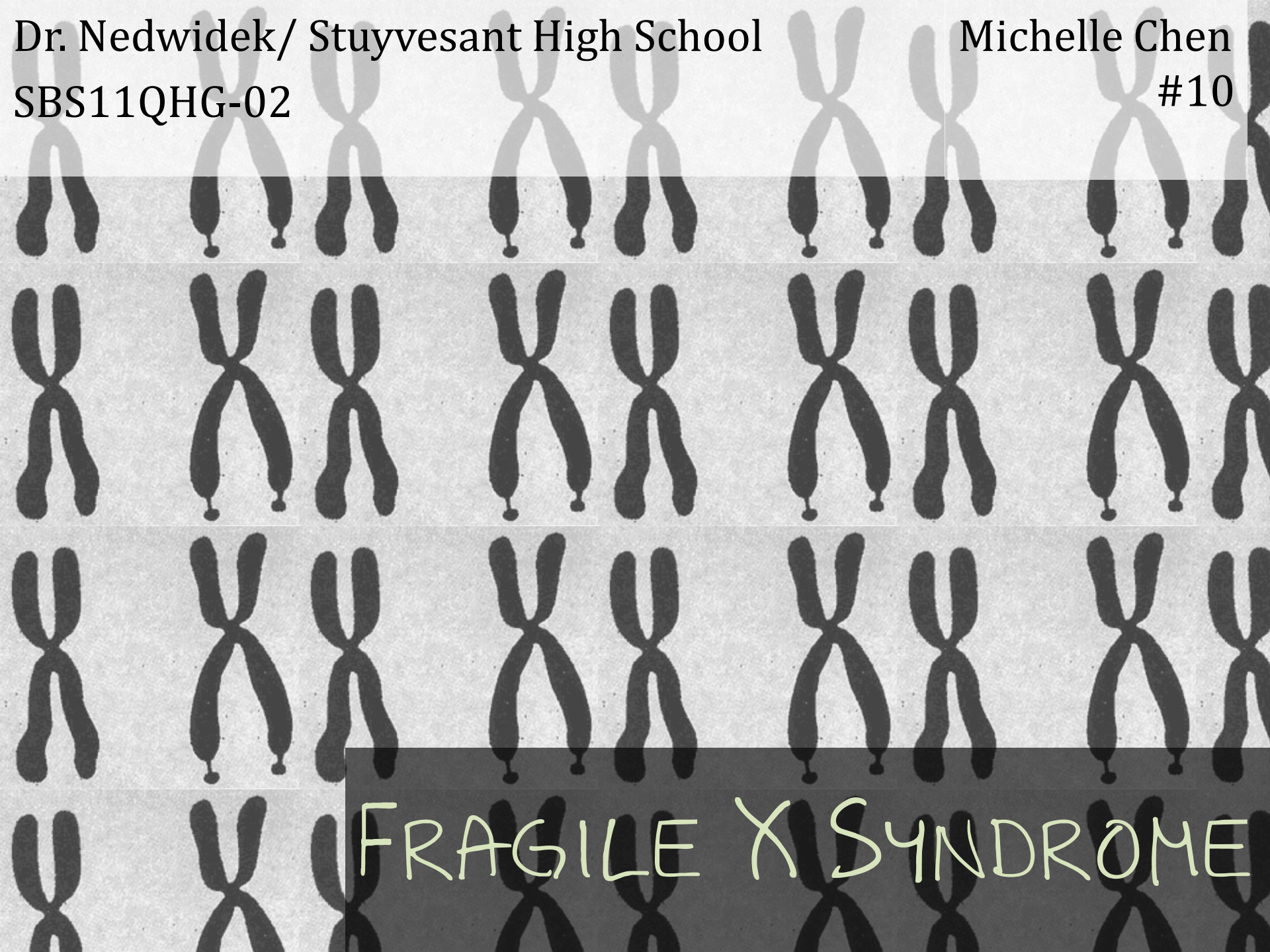
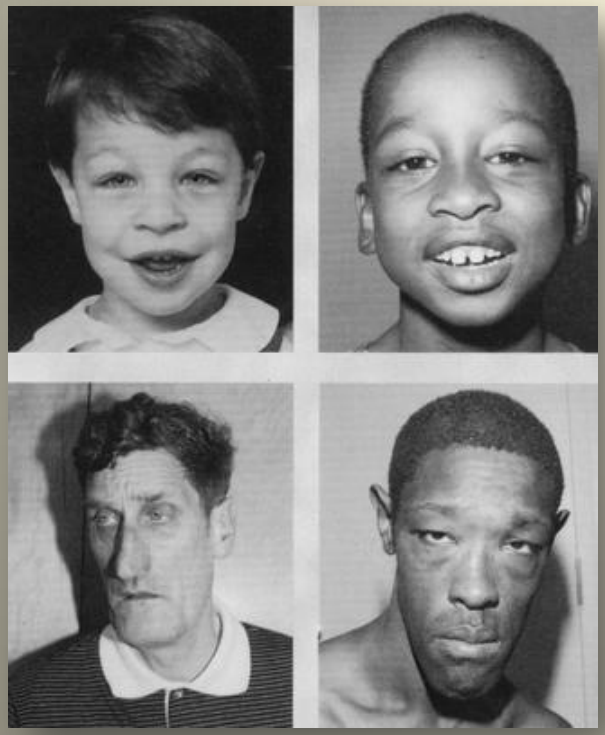
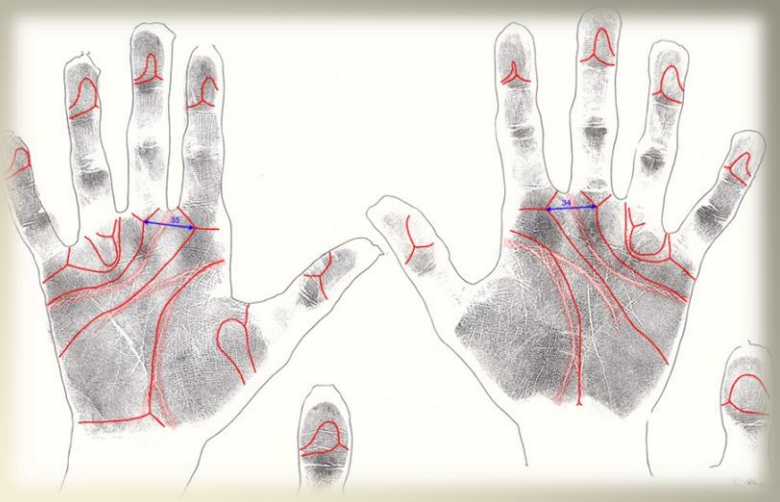


Fragile X Syndrome

Physiology

•Fragile X Syndrome is a X-linked dominant disease.
•It has an early onset
•No effect on lifespan, so it is often inherited from parents . It can be spontaneous as well, but it is not as common.
•Common cause of autism

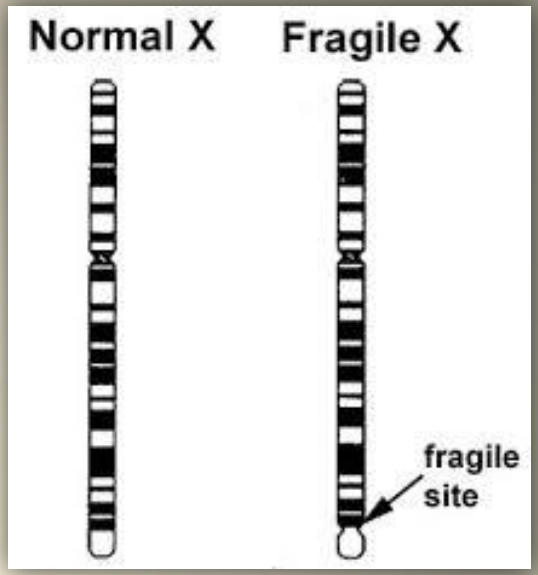




Symptoms

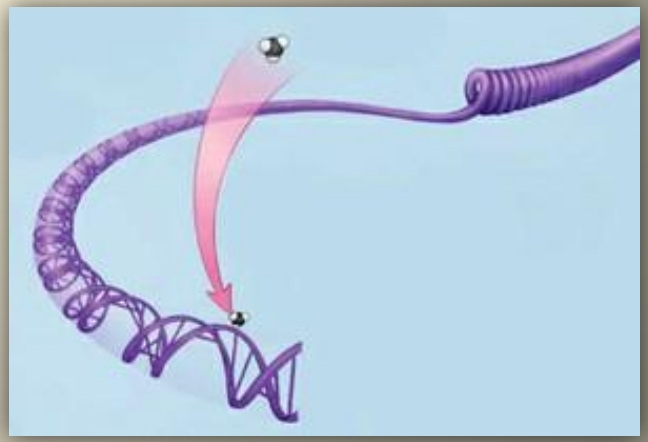
•Behavioral symptoms include mental retardation, inability to maintain eye contact, motor delay, and cognitive delay. These symptoms are present at birth.
•Physical phenotypes include a long face, a large forehead, a large body, and more. These symptoms start showing at puberty.
•Because it is x-linked, girls usually get only one mutated X chromosome. Since most females still have a normal X chromosome, X chromosome inactivation allows some cells to express the normal chromosome. Therefore, symptoms in girls are not as severe as symptoms in males, who only have one X chromosome.

Molecular Cause



•There are two ways a person can get Fragile X. The more common is an expansion of a sequence of CGG nucleotides in the FMR1 gene. 1% of patients have a mutation where FMR1 is partially or fully deleted.
•For patients with expansions, the more expansions there are, the more severe.
•An expansion of over 200 repeats is a full mutation. Most males have a full mutation while females are usually mild patients.

•FMR1 makes FMRP, a protein that adapts synapses so that nerve cells can communicate. It is also a chaperone for messenger mRNA. A chaperone helps fold large proteins and prevents the proteins from sticking to each other.
•It is also found in ovaries and testes, but function is not known.
•When there is an expansion, FMR1 is turned off due to instability in CGG expansion regions and FMRP is not produced. When there is an mutation, insufficient amounts of FMRP are made.



Treatments/Risks and Limits

•There are special clinics for fragile x syndrome. They provide families with information about most up-to-date therapies and medications.
•The first step in treatment is finding a counselor so that the patient can be tested for specific symptoms. A support plan and education plan is then made specifically for the patient.
•Fragile X patients meet requirements for special education services under federal law. They have special counselors who walk them to classes to ensure safety.
•Popularly prescribed medicine include antidepressants, antipsychotics, and stimulants
•Therapies under study include fenobam, which relieves anxiety and hyperactivity. It must b tested for safety and aftereffects

Limits:
•There is no way to find all of a patient's symptoms, so not all symptoms can be alleviated.
•Fragile X students may still struggle in school despite their special education plan.
•Medicine may cause side effects.

Proposed Cure/Limits

•In fragile X patients, the FMR1 gene is silenced due to instability in CGG expansion regions.
•Epigenetics is the study of gene expression. In this field, there have been many advancements such as azacitidine. It has been found that this drug can reactivate tumor-suppressing genes so that tumor development decreases. This drug is often injected into leukemia patients.
•Other studies show that enhancers play a big part in gene regulation. It has been found that if an enhancer and the desired gene is combined and then inserted into an organism, the enhancer can later be used to activate the gene.
•My proposed cure is to have a drug, like azacitidine, developed to reactivate the FMR1 gene when it is silenced.

Limits:
•It may be difficult to keep FMR1 activated because CGG regions are still unstable.
•This would not help patients with mutations in the FMR1 gene.
•Since this disease is not lethal, patients have a normal life span. If a treatment causes death or more symptoms, the treatment is not worth the risk.

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