Genetic Testing for Wilson Disease

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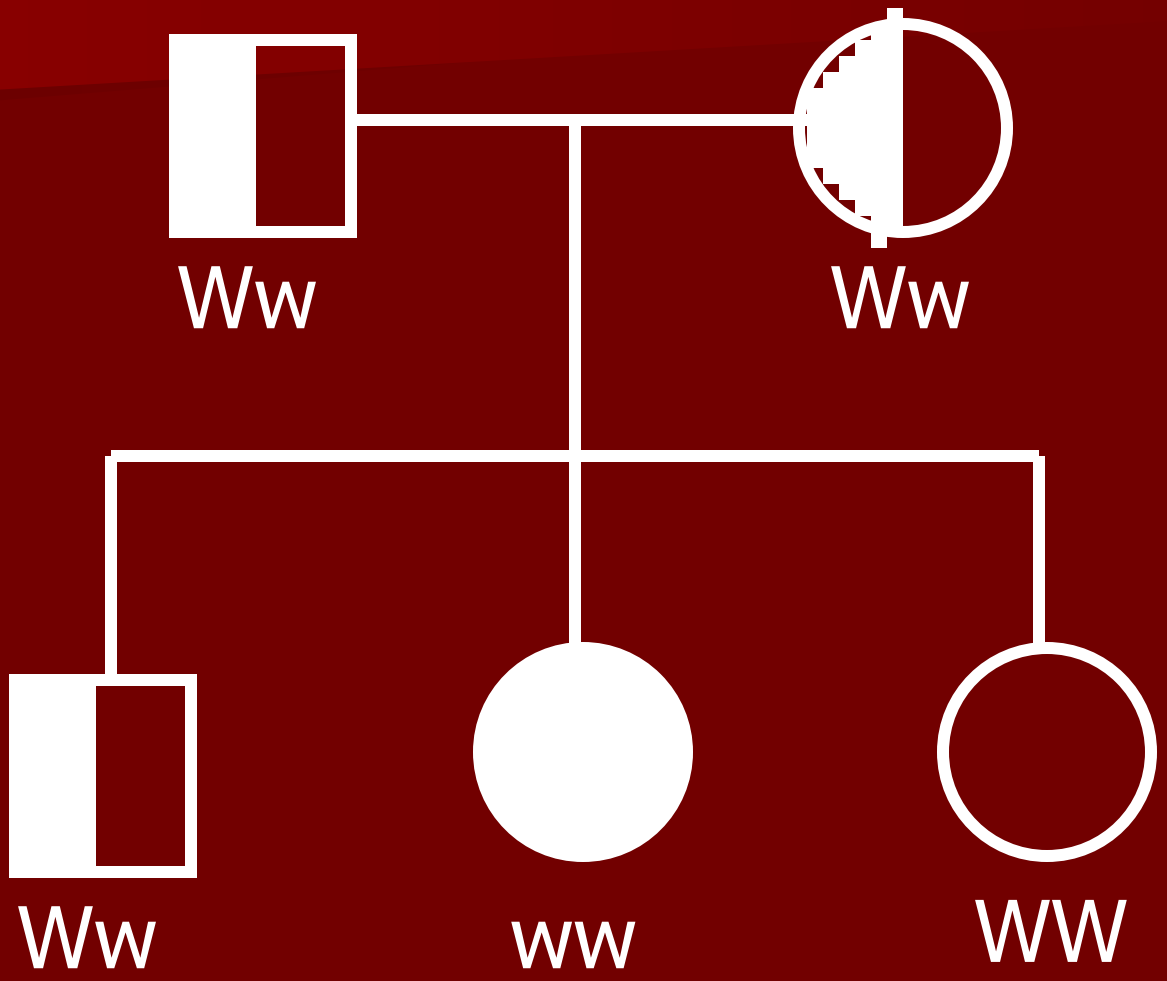
What Causes Wilson Disease?

- Wilson disease is caused by mutations in the *ATP7B* gene.
- This gene makes an enzyme that is involved in copper transport.
- When the enzyme is mutated (not working properly) copper accumulates in the liver and brain and becomes toxic.

How Does it Run in Families?

- Wilson disease is inherited in an autosomal recessive pattern.
- Affected individuals have mutations in both copies of *ATP7B*
- Carriers (mutation in only one copy) do not have symptoms

How Does it Run in Families?



Current US Clinical Testing for Wilson Disease

- The University of Chicago
- Ambry Genetics
- Boston University School of Medicine
- Mayo Clinic
- Prevention Genetics
- Seattle Children's Hospital
- University of Oklahoma Health Sciences Center

www.dnatesting.uchicago.edu

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Genetic Testing for Wilson Disease (WD)

Information for Patients and Families

What do I need to know about testing for Wilson disease?

Wilson disease (WD) is caused by a change in someone's DNA. People with WD can have liver problems, abnormal movements, seizures, and psychological problems. This blood test may prove that you have WD. However, some people with WD will have a negative result, so this test will not rule out WD. There is also a chance that the test will find something that we do not understand. Thus, we may need to test other family members to learn more. This information sheet will provide more details about WD and this testing. Please talk to a genetic counselor, if you have more questions about testing.

What is Wilson disease?

Wilson disease is a rare genetic condition that affects how copper is used in our body. It leads to three main types of symptoms:

- Liver problems–jaundice, hepatitis, cirrhosis, enlarged liver, and anemia
- Neurological problems–tremors, poor coordination, muscle spasms, and seizures
- Psychiatric problems–depression, mood changes, personality changes, and psychosis

Kayser-Fleischer rings are copper deposits that form a ring surrounding the cornea of the eyes. These are only found in patients with WD and are diagnostic for this disease. Patients will start showing signs of WD at 3 to 45

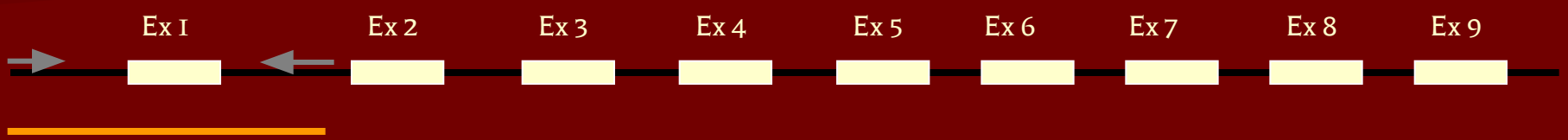
Our Test . . .

- Full gene sequencing of coding region of *atp7b* (21 exons)
  - Cost: $2025
  - TAT: 4 - 6 weeks

DNA extraction

- Process of getting DNA from a blood, saliva, or other body tissue.
- http://learn.genetics.utah.edu/content/labs/extraction/

Targeting ATP7B



- Need to PCR amplify each exon (21) of ATP7B before sequencing

PCR Amplification

- Reproduce only the parts of DNA (exons of ATP7B) that you are interested in.
- http://www.youtube.com/watch?v=HMC7c2T8fVk

DNA Sequencing

- Reading the DNA code within the *ATP7B* gene to look for any changes.
- Cycle sequencing animation
- http://www.youtube.com/watch?v=ezAefHhvecM

Ordering Testing

- A physician must order the test
- We recommend that a geneticist or genetic counselor be involved in ordering testing
  - Finding a genetics clinic or GC—
    - www.genetests.org
    - www.nsgc.org
- They will fill out the appropriate paperwork and arrange for blood sample to be sent to The University of Chicago

Ordering Testing

- Test report will be faxed to referring physician
- Geneticist/GC can explain results and implications to family
- Questions? —Please contact me!
  - Melissa Dempsey, MS

    The University of Chicago

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Insurance/Billing

- The University of Chicago will bill your insurance company or accept payment by check or credit card.
- All insurance companies are different, but most of them should cover at least part of the cost of testing.
- CPT (Current Procedural Terminology) codes:
  - Insurance companies use these codes to define the method of testing.
  - For *ATP7B* testing: 83891, 83898 x 4, 83904 x 9, 83912 .

Possible Results:

- 2 mutations detected:
  - confirms diagnosis of Wilson Disease.
  - allows for easy testing of other family members, who may want testing.

Possible Results:

- 1 mutation detected:
  - does not confirm or rule out Wilson Disease
    - patient may have 2nd mutation that wasn't detected
    - Patient may be a carrier of WD and have some other reason for their symptoms
    - ~1/90 individuals are carriers of WD.

Possible Results:

- No mutation detected:
  - does not rule out the diagnosis.
  - ~98% of people with WD will have mutations identified.
  - If diagnosis is doubtful, a negative result leans against the diagnosis, and other possible diagnoses should be considered.

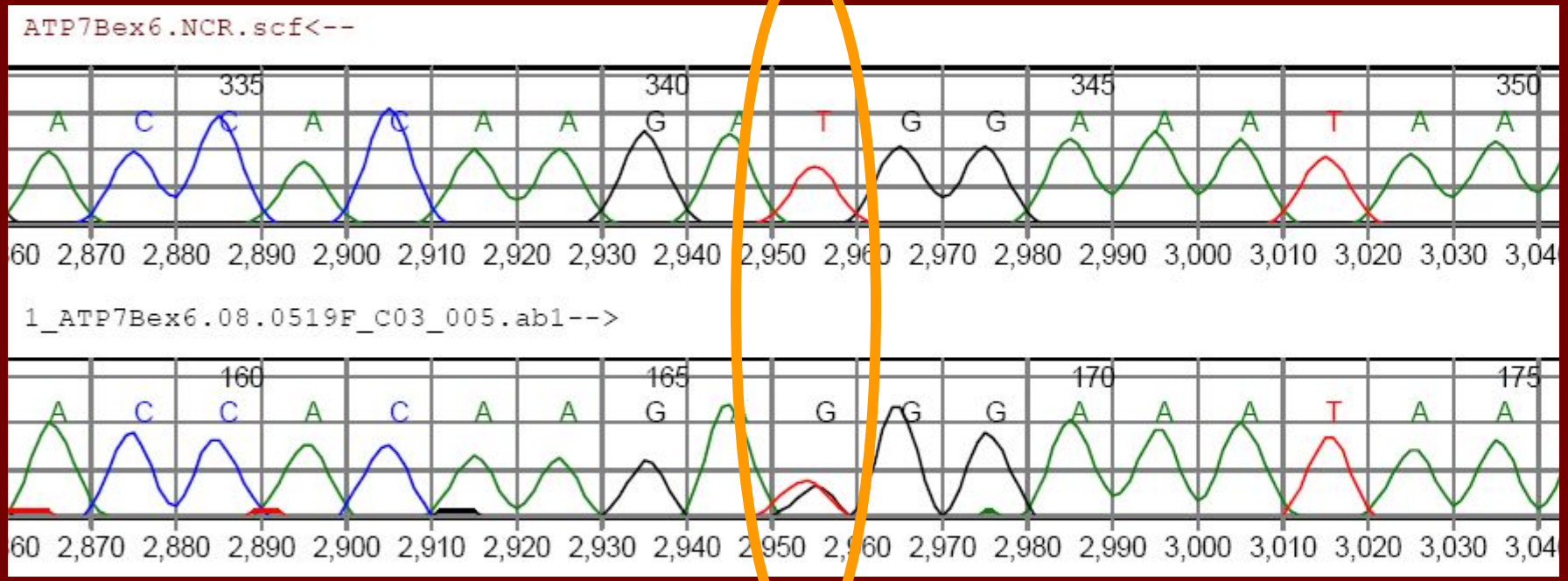
Possible Results:

- Variant of unknown significance:
  - A small number of people will have a change in the gene, but we do not know what the change means
  - May recommend testing other family members to try to figure it out.

Case #I

- I2 year old female with abnormal copper levels

Exon 6

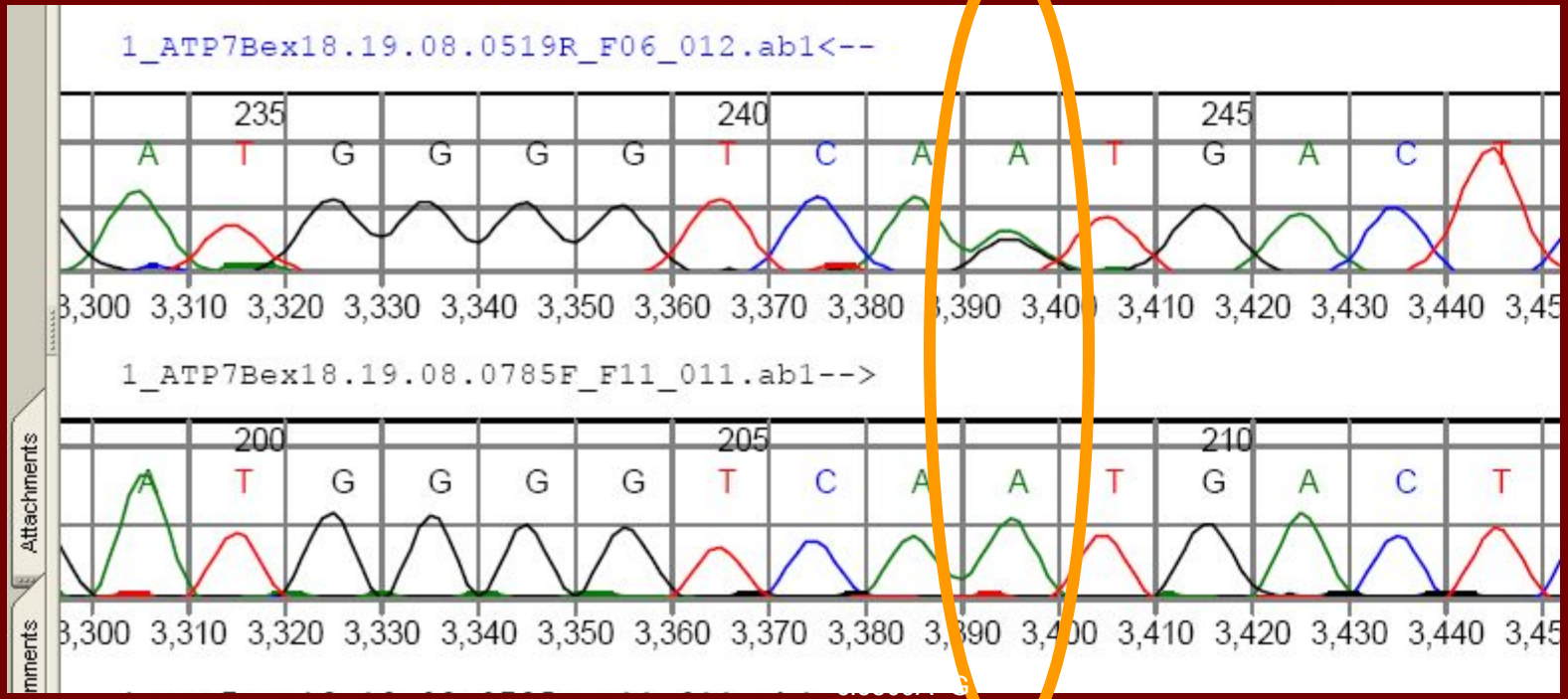


c.1934T>G (p.M645R)

Case #1

- 12 year old female with abnormal copper levels

Exon 18

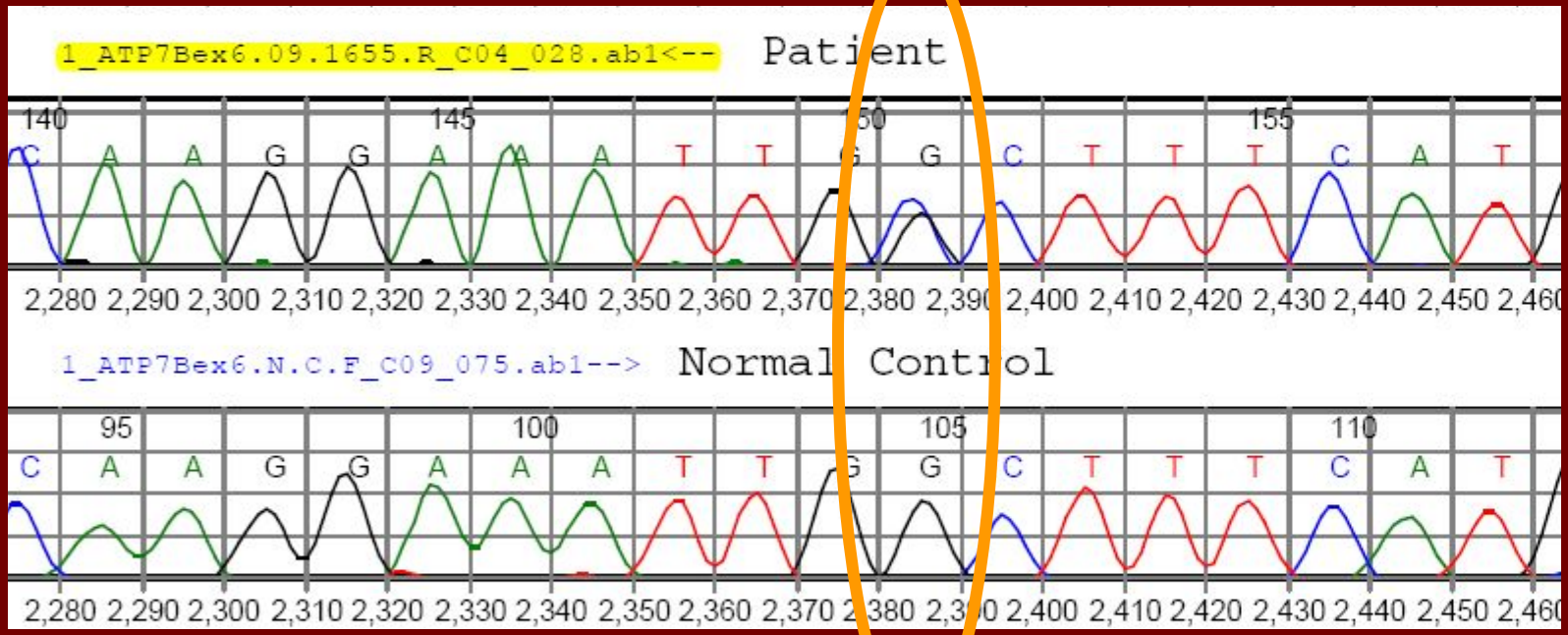


c.3809A>G (p.N1270S)

Case #2

- 12 year old male with atypical symptoms
- Single mutation detected

Exon 6



c.1877G>C (p.G626A)