What is Wilson’s disease?
- An inherited disorder
- Excessive amounts of copper accumulate in the body
  - liver
  - brain
  - eyes

Symptoms
- Yellowing of the skin or the whites of the eye (jaundice)
- Fatigue
- Loss of appetite
- Abdominal swelling
- Psychiatric or nervous system problems in young adults
- Clumsiness, trembling, difficulty walking, speech problems, deteriorating school work, depression, anxiety, and mood swings
- Copper deposits form a green-to-brownish ring, called the Kayser-Fleischer ring, around cornea (in eye)
- Abnormalities in eye movements
Who is affected

- 1 in 30,000 individuals
- Signs and symptoms first appear between the ages of 6 and 40, but most often begin during the **teenage years**

How is it inherited?

- **Autosomal recessive pattern**
  - both copies of the gene in each cell have mutations.
  - Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene
    - They typically do **not** show signs and symptoms of the condition

Mutations

- Mutations in the **ATP7B** gene cause this disease.
- Normal variations in the **PRNP** gene modify the course of Wilson disease.
- The **ATP7B** gene
  - provides instructions for making a protein
    - Plays a role in the transport of copper from the liver to other parts of the body.
    - Particularly important for the elimination of excess copper from the body.
  - Mutations in the **ATP7B** gene **prevent** the transport protein from functioning properly
    - Due to the shortage of functional protein, excess copper is **not removed** from the body.
    - Copper accumulates to **toxic levels** that can damage tissues and organs, particularly the liver and brain.
    - This explains why the symptoms occur
  - A normal variation in the **PRNP** gene may delay the age of onset of Wilson disease and affect the type of symptoms that develop.
**PRNP: More Details**

- The PRNP gene provides instructions for making prion protein, which is active in the brain and other tissues.
- **Transferring copper**
  - Studies have focused on the effects of a PRNP gene variation that affects the prion protein at position 129.
  - At this position, the protein building block (amino acid) methionine or valine is used.
  - Onset of symptoms of Wilson disease is delayed by several years if person has methionine (instead of valine) at position 129 in the prion protein.
  - Also may increase symptoms that affect the nervous system (tremors).
- Larger studies needed to establish effects of this PRNP variation

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**Charts**

- **Genomic regions, transcripts, and products**
- **Genomic context**

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**Chromosome**

- **Chromosome:** 13
- **Location:** 13q14.3

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**NCBI links, etc**

  - That's for NM_001005918.1. The other is NM_000053.2.
- Involved in the export of copper out of the cells
Animal to study
- This disease can be studied in rats
- The e-value is $2 \times 10^{-13}$
- When you compare the protein sequences using BLAST, you find that the human protein sequence is homologous with the sequence in rats
- Although this is not very low of a value, the sequences are 95% identical, which makes me confident that this would be an appropriate test animal
- The reason the e-value is so low is because the protein sequence is short

Diagrams
- Provided by http://www.hcforum.fr/eurowilson/?page=0&lang=it
More information:

- **Treatment**
  - American Association for the Study of Liver Disease. Diagnosis and Treatment of Wilson Disease.
  - GeneCards
  - MedlinePlus - Health Information (search)
  - Additional NIA Resources - National Institutes of Health (3 links)
  - Educational Resources - Information pages (3 links)
  - Patient Support - For patients and families (5 links)
  - GeneReview - Clinical summary
  - GeneTests - DNA tests ordered by healthcare professionals
  - Genetics Home Reference - Linking patients to medical research
  - PubMed - Recent literature
  - Online Books - Medical and science texts
  - Simons’ Online Mendelian Inheritance in Man (OMIM®): Disorders of Copper Transport
  - OMIM - Genetic disorder catalog

- More questions:
  - See How can I find a genetics professional in my area? in the Handbook.
  - Ask the Genetic and Rare Diseases Information Center.
  - Submit your question to Ask the Genetiiccist.
  - What does it mean if a disease appears to run in my family?
  - What are the different ways in which a genetic condition can be inherited?
  - If a genetic disorder runs in my family, what are the chances that my children will have the condition?
  - Why are some genetic conditions more common in particular ethnic groups?
  - Genetics and Health
  - Resources for Patients and Families
  - Resources for Health Professionals

Links provided by Genetics Home Reference

Bibliography

- [http://www.hcforum.fr/eurowilson/?page=0&langue=it](http://www.hcforum.fr/eurowilson/?page=0&langue=it)
- [http://www.genecards.org/](http://www.genecards.org/)
The End!