Variations on a gene: investigating the genetic basis of iron overload

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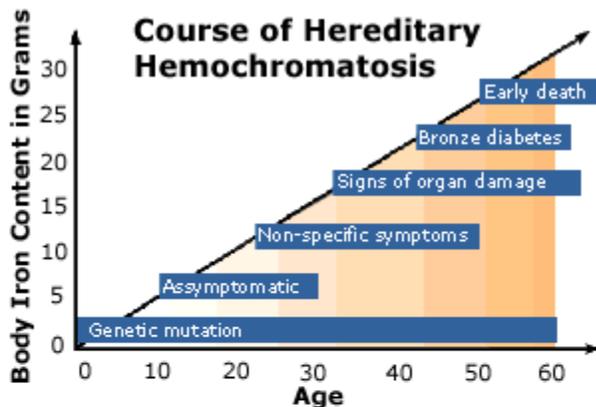

Chart reflecting the course of hereditary hemochromatosis This graph depicts the clinical course of iron overload due to hereditary hemochromatosis. The Y axis reflects increasing amounts of iron concentration in the body and the X axis reflects increasing age in years from birth to age 60. The diagonal line shows that as a person's iron concentration increases over time, the effects of iron on the body are initially seen as non-specific symptoms, followed by more serious signs of organ damage, bronze diabetes, and ultimately early death.

Slope depends on individual.

Hereditary hemochromatosis is a common disease that results in the accumulation of iron in the body. Approximately 5 per 1000 Americans inherit this disorder, but symptoms may never appear, leaving many people undiagnosed.

Mutations of the *HFE* gene are commonly at fault. In this tutorial, we examine the link between SNPs of the *HFE* gene and the development of disease. In the course of deciphering whether a SNP is significant, we look to see whether the SNP causes an amino acid change, the nature of this change (e.g., a switch of cysteine to another amino acid may disrupt a disulfide bond), and whether this change takes place in a conserved domain. We also take a look at the amino acid change on a three-dimensional representation of the HFE protein structure.

So... can a switch of a single nucleotide be responsible for a mutant HFE protein that allows iron regulation to go astray?

Important Links

Live PubMed searches
(1) Hemochromatosis
(2) HFE and single nucleotide polymorphism
(3) REVIEWS

Additional resources
OMIM

LocusLink

Map View

Genes and Disease [http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?call=bv.View..ShowSection&rid=gnd.section.251]

Hospital Practice [http://www.hosppract.com/genetics/9908mmc.htm]

Box: Search the SNPs database for HFE

Do single nucleotide polymorphisms in the *HFE* gene have functional consequences?

For this tutorial, you will need to have flash [http://www.macromedia.com/go/getflashplayer] installed on your computer.

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