PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Iron overload lifted

ArticleInfo		
ArticleID	:	4889
ArticleDOI	:	10.1186/gb-spotlight-20031201-01
ArticleCitationID	:	spotlight-20031201-01
ArticleSequenceNumber	:	241
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	1
ArticleHistory	:	RegistrationDate : 2003–12–1 OnlineDate : 2003–12–1
ArticleCopyright	:	BioMed Central Ltd2003
ArticleGrants	:	
ArticleContext	:	130594411

Cathy Holding
Email: cholding@hgmp.mrc.ac.uk

On its own, genomic DNA sequence is usually insufficient to elucidate the mechanisms of human disease, but in the November 30 Nature Genetics, George Papanikolaou and colleagues at the National and Kapodistrian University of Athens Medical School report the genetic cause of juvenile hemochromatosis that would have benefited from the accurate genome sequence in the first place (*Nature Genetics* 2003, DOI:10.1038/ng1274).

This severe disease is linked to the centromeric region of chromosome 1q, but according to Papanikolaou et al., the published genomic region contains 'numerous gaps and duplications' that required them to rely on previously existing sequence contigs and to produce their own interpretation of the genome assembly, during attempts to carry out positional cloning. This led to the identification of different mutations in a single gene in a location that accounts for all of the juvenile hemochromatosis alleles found in one French, one Canadian, and 10 Greek families. This single piece of information confirms predicted mechanisms of hemochromatosis as well as of another iron uptake disorder, anemia of inflammation.

Papanikolaou *et al*. examined samples from the 12 unrelated families with the disease and confirmed linkage to the 1q21 locus, also known as HFE2, and they also confirmed absence of mutation in the previously implicated gene encoding hepcidin. Multiple mutations were observed in the transcription unit LOC148738 during sequencing that were absent in over 500 control chromosomes. A common mutation - termed the G320V missense variant - was observed in seven Greek families sharing the common Greek haplotype as well as in the Canadian and French families. A full-length transcript termed hemojuvelin from a 4265-bp region of chromosomal DNA was predicted to result in five spliced isoforms, containing protein domains consistent with a role as a membrane-bound receptor or secreted hormone. Comparative genome analysis revealed 85% homology to mammalian orthologues and the similarity of one isoform to the human and chick repulsive guidance molecule of unknown function. Hepcidin levels were monitored in urine and were depressed in affected family members, suggesting a role for hemojuvelin in modulating its transcription.

"The identification of hemojuveline presents new therapeutic and diagnostic opportunities for the management of iron-related disorders," the authors conclude.

References

1. *Nature Genetics*, [http://www.nature.com/ng]

2. National and Kapodistrian University of Athens Medical School, [http://www.surgery.gr/]

3. Ironing out hemochromatosis heterogeneity

4. Hepcidin, a key regulator of iron metabolism and mediator of anemia of inflammation