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Sequence of the major histocompatibility complex

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Abstract

The entire human major histocompatibility complex (MHC), a genomic region critical for immune defense, has been sequenced.

Significance and context

The sequencing of the MHC is part of the publicly funded human genome project to systematically sequence human chromosome 6, which began at the Sanger Centre near Cambridge, UK in 1996. The MHC region at human chromosome 6p21.31 contains the genes for numerous proteins involved in the functioning of the immune system, the best known being the highly polymorphic MHC class I and II glycoproteins. These present antigens to T cells to initiate an immune response, and are the main target of rejection reactions in transplantation. The genes for the MHC class I and class II molecules (also known as human leukocyte antigens, HLA) are respectively clustered in two distinct regions; the region between, known as the class III region, contains a variety of genes, including some that encode immunologically relevant proteins. The MHC is associated with susceptibility to many autoimmune diseases (for example, rheumatoid arthritis and diabetes).

Key results

The complete sequence of the MHC region spans 3,838,986 base-pairs. It is the achievement of an international consortium including laboratories in the University of Washington, USA and Tokai University, Japan and represents a patchwork of different haplotypes. The MHC contains 224 identified gene loci, approximately half of which are predicted to be expressed. This is an average of one gene per 16 kilobases, which makes the MHC one of the most gene-rich regions of the genome sequenced so far. Some 41% of these genes were identified as a direct result of the genome sequencing effort. In addition to the polymorphic MHC class I and II molecules, the MHC encodes many other proteins involved in immune defense, including the TAP proteins (transporters associated with antigen processing), the inflammatory cytokine tumor necrosis factor (TNF) and components of the complement system. Nearly 40% of the expressed MHC genes relate to immune function.

Links

The complete human MHC sequence and further information is available from the [Sanger Centre](#).

Conclusions

It is hoped that the MHC sequence information, and comparison with further sequencing of common haplotypes, will provide important insights into the biology and evolution of multigene families and the identification of disease loci.

Reporter's comments

The simultaneous publication of the complete sequence of the chicken MHC (in the same issue of *Nature*) highlights some striking differences in the evolution of the MHC in mammals and birds. The chicken MHC is 92,000 base pairs long and contains just 19 genes (around one-twentieth the size of the human MHC). The analysis of MHC regions from other haplotypes and other vertebrates will provide further insights into MHC-associated immune defense and disease.

Table of links

Nature

[The complete human MHC sequence](#)

[Sanger Centre](#)

References

1. consortium The MHC sequencing: Complete sequence and gene map of the major histocompatibility complex. *Nature*. 1999, 401: 921-923. 0028-0836