

Horton et al. (2004)
Gene Map of the Extended Human MHC
Nature Review Genetics 5:889-899

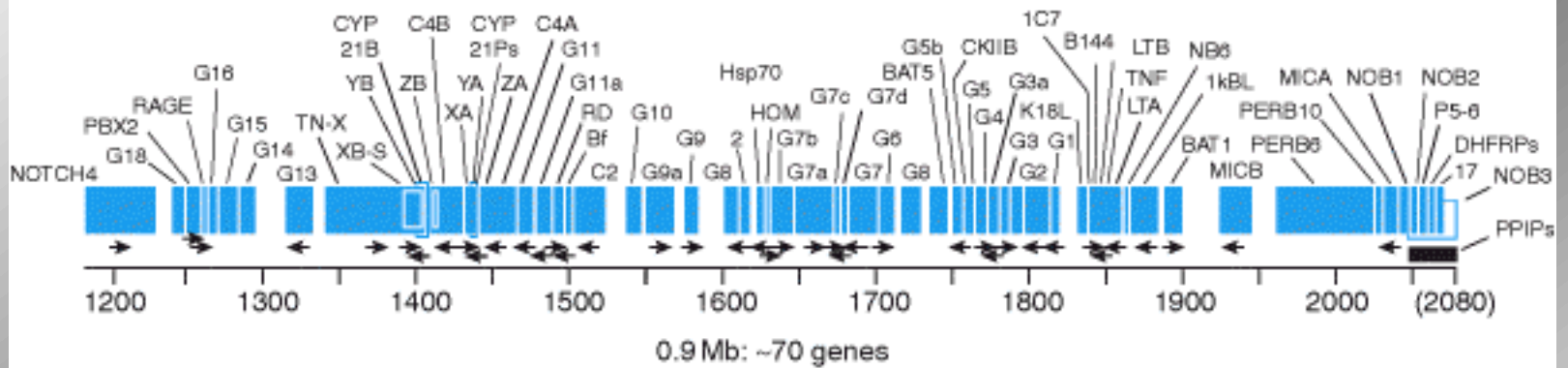
MHC = Major Histocompatibility Complex

oppure

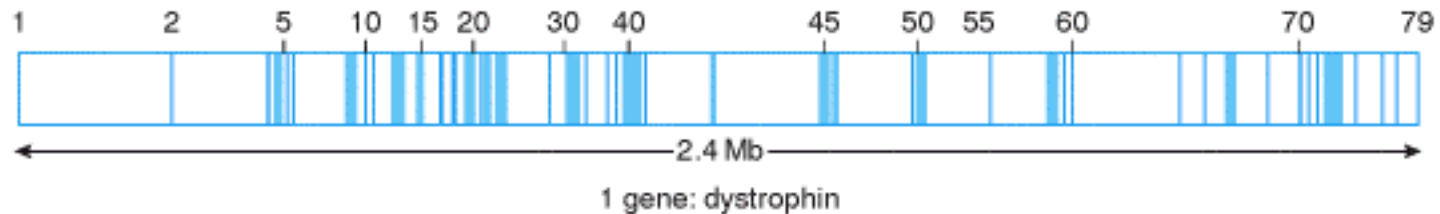
HLA complex = Human Leucocyte Antigen complex

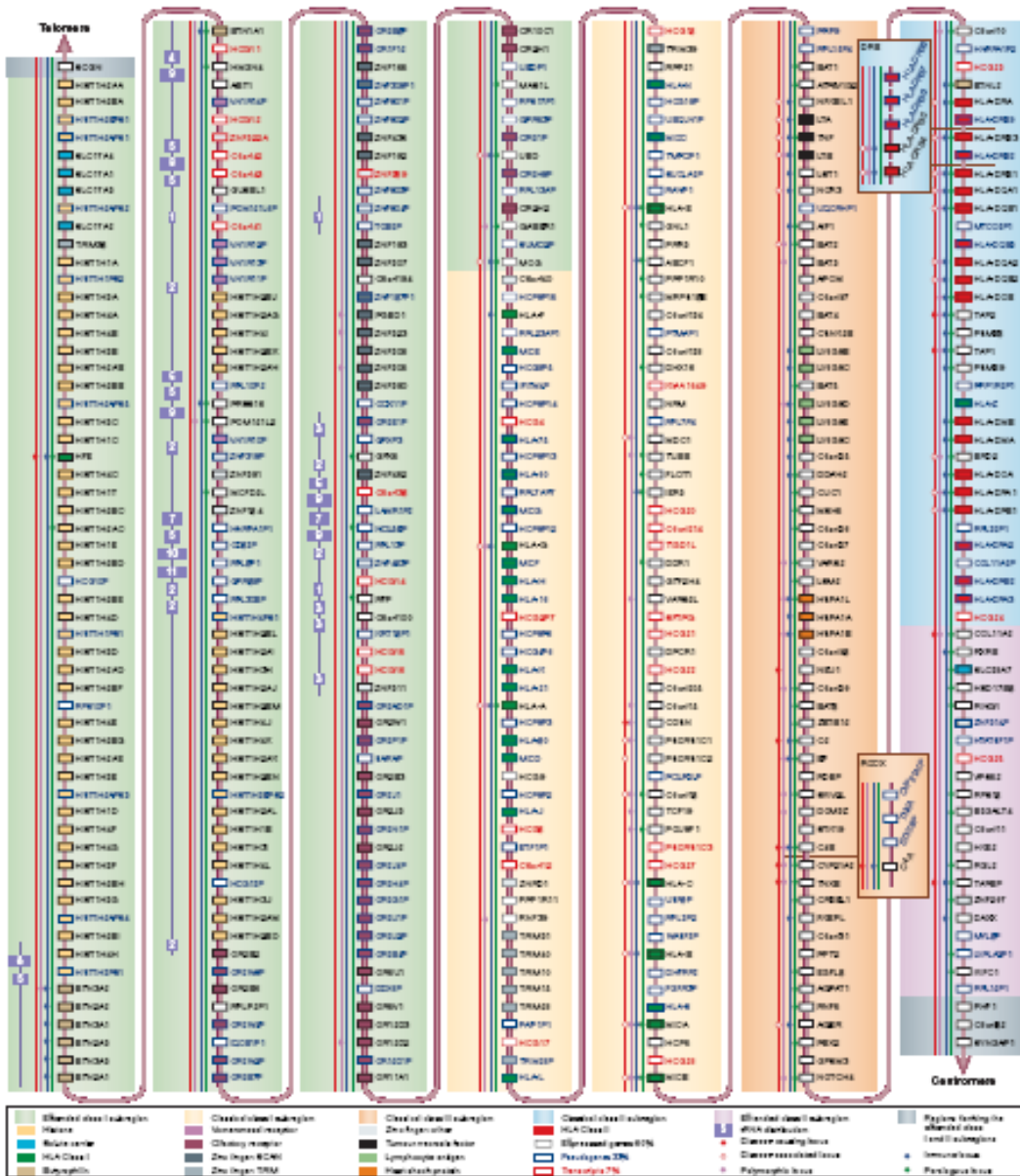
La funzione primaria delle molecole MHC è quella di conferire protezione contro patogeni

(A)



(B)





Human Extended MHC (xMHC)

Cromosoma 6
7.6 Mb

421 loci
252 (60%) geni
espressi (cDNA)
30 (7%) trascr
(EST; no ORF)
139 (33%)
pseudogeni



Supercluster degli istoni.
Proteine coinvolte nella
formazione dei nucleosomi

Supercluster dei geni
HLA di classe I classici:
HLA-A; HLA-B e HLA-C
e quelli non classici
HLA-E; HLA-F e HLA-G

che presentano, insieme alla $\beta 2$ -microglobulina (B2M), gli antigeni alle cellule T CD8+ e sono coinvolti nella risposta immunitaria mediata dalle cellule natural killer

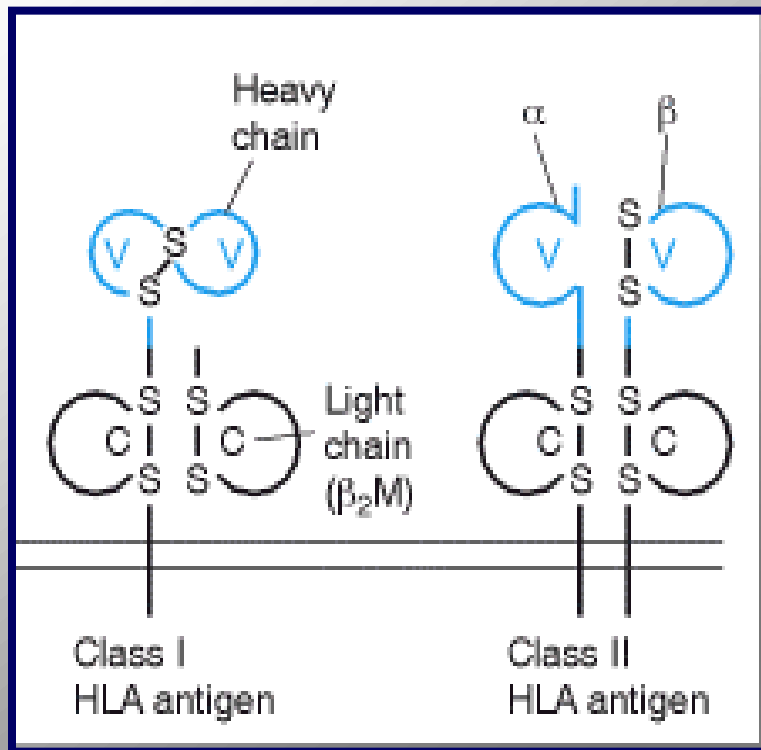


Cluster dei geni HLA di classe II classici:

HLA-DP; HLA-DQ e HLA-DR

e quelli non classici

HLA-DM; HLA-DO



I geni di classe II sono espressi sulla superficie delle cellule come eterodimeri, una catena α e una β e presentano gli antigeni alle cellule $CD4^+$

I geni HLA di classe I e di classe II sono altamente polimorfici (gene HLA-B il più polimorfico del genoma umano)

Table 3 | **A minimal set of immune-system genes in the human xMHC**

Category	Genes
Antigen processing/ presentation	<i>HLA-A, -B, -C, -DMA, -DMB, -DOA, -DOB, -DPA1, -DPB1, -DQA1, -DQA2, -DQB1, -DQB2, -DRA, -DRB1, -DRB3, -DRB4, -DRB5; PRSS16; PSMB8, PSMB9; TAP1, TAP2, TAPBP; UBD</i>
Immunoglobulin superfamily	<i>AGER; BTN1A1, BTN2A1, BTN2A2, BTN2A3, BTN3A1, BTN3A2, BTN3A3, BTNL2; C6orf25; MOG</i>
Inflammation	<i>ABCF1; AIF1; DAXX; IER3; LST1; LTA, LTB; NCR3; TNF</i>
Leukocyte maturation	<i>DDAH2; LY6G5B, LY6G5C, LY6G6D, LY6G6E, LY6G6C</i>
Complement cascade	<i>BF; C2, C4A, C4B</i>
Non-classical MHC class I	<i>HLA-E, HLA-F, HLA-G; HFE</i>
Immune regulation	<i>NFKBIL1, RXRB, FKBPL</i>
Stress response	<i>HSPA1A, HSPA1B, HSPA1L; MICA, MICB</i>

Most of these genes have established functions for innate or adaptive immunity; genes with remote links have been excluded. Some genes have been included because they are related by sequence to a known immune gene family but the precise function of these is still to be determined. The largest class of immune system genes is involved with antigen processing and presentation, and includes classical class I and II molecules, as well as some of the antigen processing machinery for loading peptides onto class I molecules. xMHC, extended major histocompatibility complex.

Mutazioni di questi geni sono associati a molte malattie genetiche e/o sono predisponenti a malattie

Table 4 | **Genes in the xMHC in which variation has a relationship to disease**

Gene symbol	Relationship to disease*
<i>xMHC extended class I region</i>	
<i>HFE</i>	Causes haemochromatosis; associated with arthropathy, multiple sclerosis, hepatocellular carcinoma
<i>UBD</i>	Associated with gastrointestinal and gynaecological malignancies
<i>MOG</i>	Associated with multiple sclerosis
<i>xMHC class I region</i>	
<i>HLA-G</i>	Associated with <i>Pemphigus vulgaris</i> in Jewish patients
<i>HLA-A</i>	Associated with autoimmune diseases; for example, birdshot chorioretinopathy
<i>HLA-E</i>	Associated with type 1 <i>Diabetes mellitus</i> ; also influences age of onset of disease
<i>MDC1</i>	Associated with inadequate DNA damage responses owing to MDC1-deficiency
<i>CDSN</i>	Causes hypotrichosis simplex of the scalp
<i>PSORS1C1</i>	Associated with psoriasis
<i>PSORS1C2</i>	Associated with psoriasis
<i>C6orf18</i>	Associated with psoriasis
<i>HLA-C</i>	Associated with autoimmune diseases; for example, psoriasis
<i>HLA-B</i>	Associated with autoimmune diseases; for example, ankylosing spondylitis or Behcet disease
<i>MICA</i>	Associated with autoimmune diseases; for example, rheumatoid arthritis and coeliac disease
<i>MICB</i>	Associated with coeliac disease

xMHC class II region

<i>HLA-DR</i> loci	Associated with autoimmune diseases; for example, rheumatoid arthritis, type 1 and type 2 <i>Diabetes mellitus</i>
<i>HLA-DQ</i> loci	Associated with autoimmune diseases; for example, narcolepsy
<i>TAP2</i>	Causes bare lymphocyte syndrome type I owing to TAP2-deficiency; associated with various diseases; for example, rheumatoid arthritis
<i>TAP1</i>	Causes bare lymphocyte syndrome type I owing to TAP1-deficiency; associated with various diseases; for example, vitiligo in Caucasian patients that are young in age at onset
<i>BRD2</i>	Associated with juvenile myoclonic epilepsy
<i>HLA-DP</i> loci	Associated with autoimmune diseases; for example, chronic beryllium disease

xMHC extended class II region

<i>COL11A2</i>	Causes autosomal dominant deafness (DFNA13) and several other diseases
<i>TAPBP</i>	Causes bare lymphocyte syndrome type I owing to TAPBP-deficiency