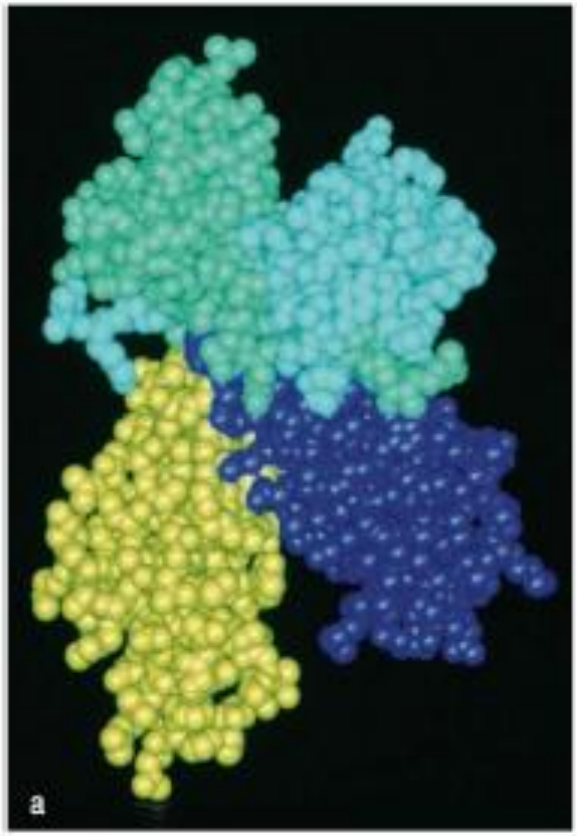
MHC Class II deficiency

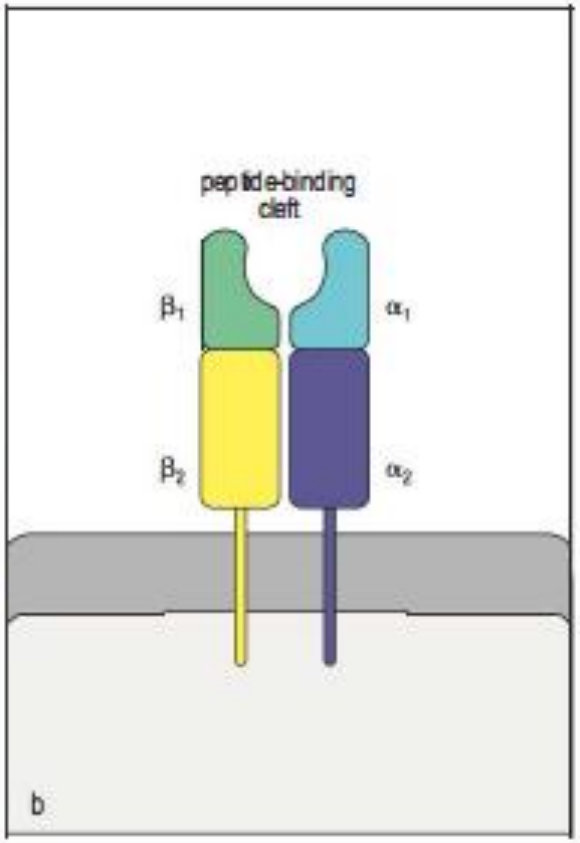
Case Study

Defect of MHC II expression

Immune cells do not express MHC class II

A mild form of SCID

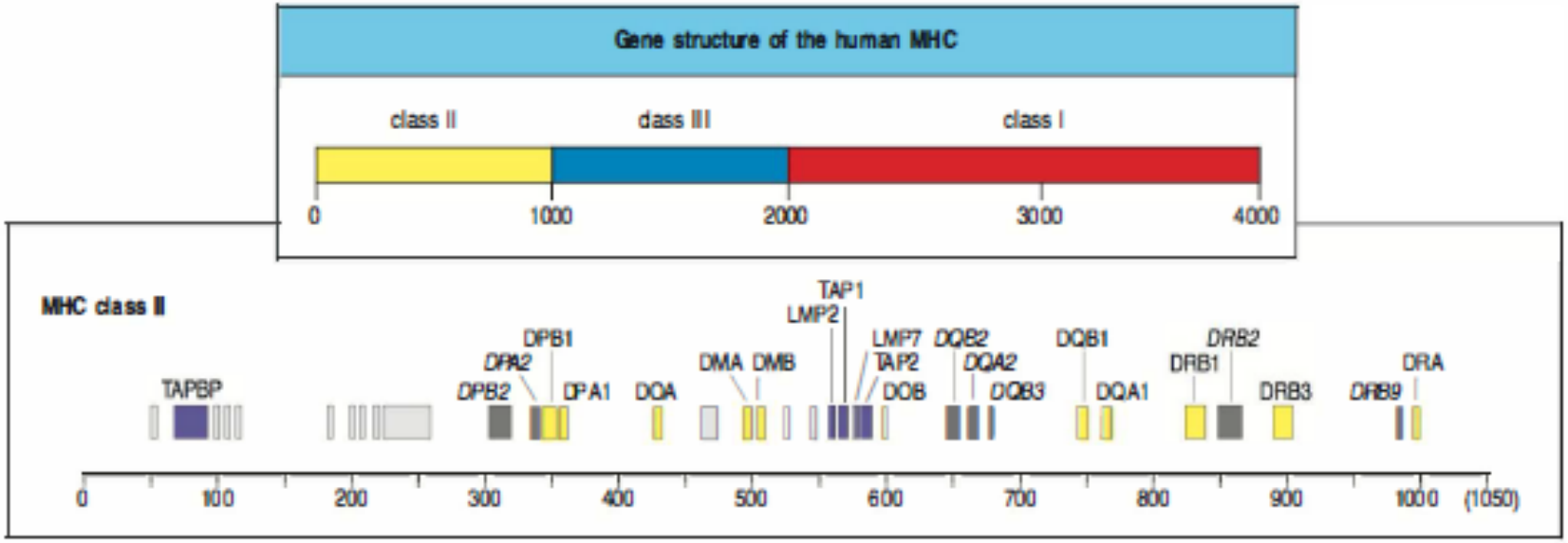




MHC II is made of a heterodimer made of one α and one β chains.

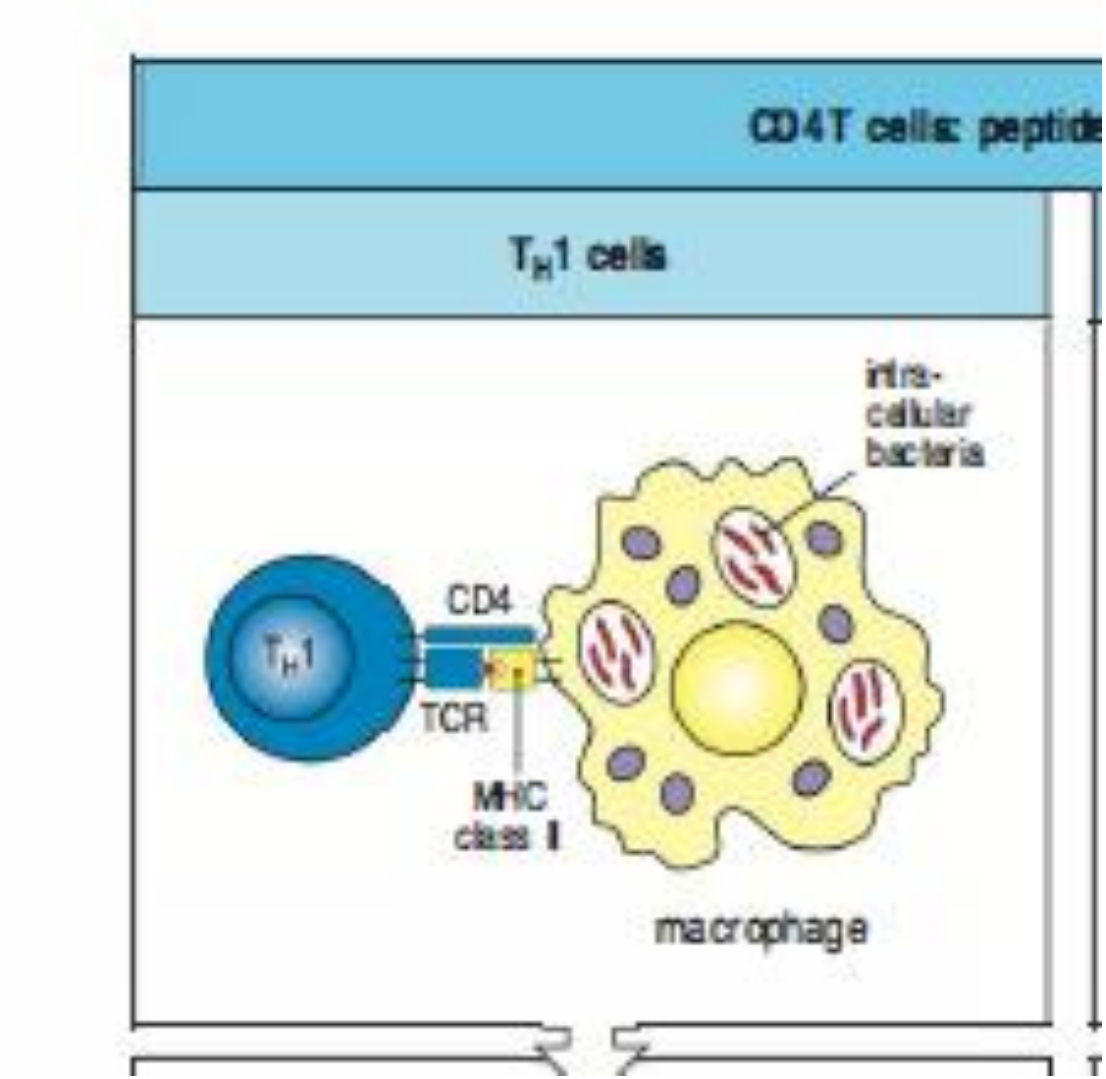
Each chain has two domains.

Peptide will bind in the cleft between both chains.



Human MHC gene codes for Class I, Class II, and Class III proteins.
Grey are pseudogenes, Yellow is MHC class II genes, and purple, genes of immune
Function not directly related to MHC I or MHC II.

MHC II genes include HLADM, HLADP, HLADQ, HLADR



Co-receptor Molecule CD4 helps stabilize the TCR-MHC II-peptide complex
CD4= T helper cell
CD8= T cytotoxic cell

Case of Helen Burns

Developed a pneumonia with severe cough and fever at 6 months of age.

Organism: *Pneumocystis carinii* ????

PHA T-cell function test (^{3}H Tritium incorporation test) to rule in/out SCID??
Allogenic B cells can be used for the assay

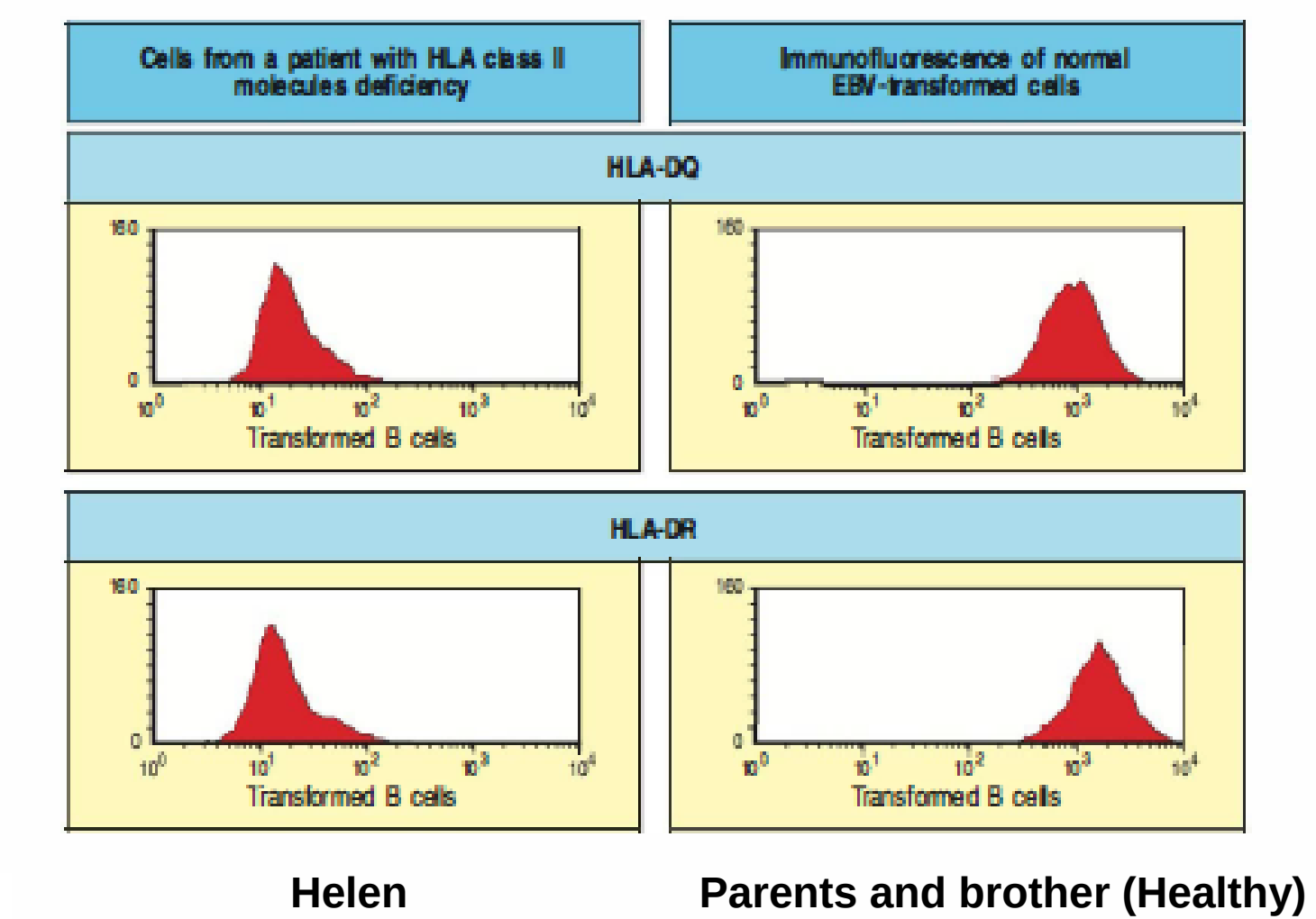
Results were normal, but proliferation was not observed in response to specific antigens (tetatnus toxin assay *in vitro*) despite patient being vaccinated for DPT.

Low IgG, IgA, and IgM levels

High WBC count (neutrophilia), low lymphocyte count. Low CD4 count, normal CD8 count.

Bone Marrow with HLA did not match with brother but matched with mother.
BM transplant was performed successfully, and immune function was restored.

Helen's B cells did not express HLA-DQ and HLA-DR



Complementation groups of MHC class II deficiency

Different causes for MHC II deficiency!

	A	B	C	D
A	–	+	+	+
B	+	–	+	+
C	+	+	–	+
D	+	+	+	–

B cell-lines isolated from different patients, fused in combination and observed for correction of MHC II expression defect.

MHC II genes are normal in these patients!
Defect in TF responsible for IFN-γ-induced MHC II expression on APCs.

Why did Helen have a low CD4 T cell count?

MHC II presence in thymic epithelial cells is crucial in CD4 T cell maturation.

Why did Helen Have low Ig levels?

Lack of CD4 help.

How was SCID ruled out?

Helen's T cells are low in numbers but normal. They can respond to non-specific mitogens such as PHA, or allogenic stimulus with Ag presented on foreign MHC.

Why no response to tetanus toxin?
Cells were unable to present it on MHC II molecules to CD4 T cells.

Would Helen reject a skin graft?

Yes. Her T cells are functional and able to recognize foreign MHC molecules on the grafted skin.

Would a SCID patient reject the skin graft?

Most likely no.