

Omenn Syndrome

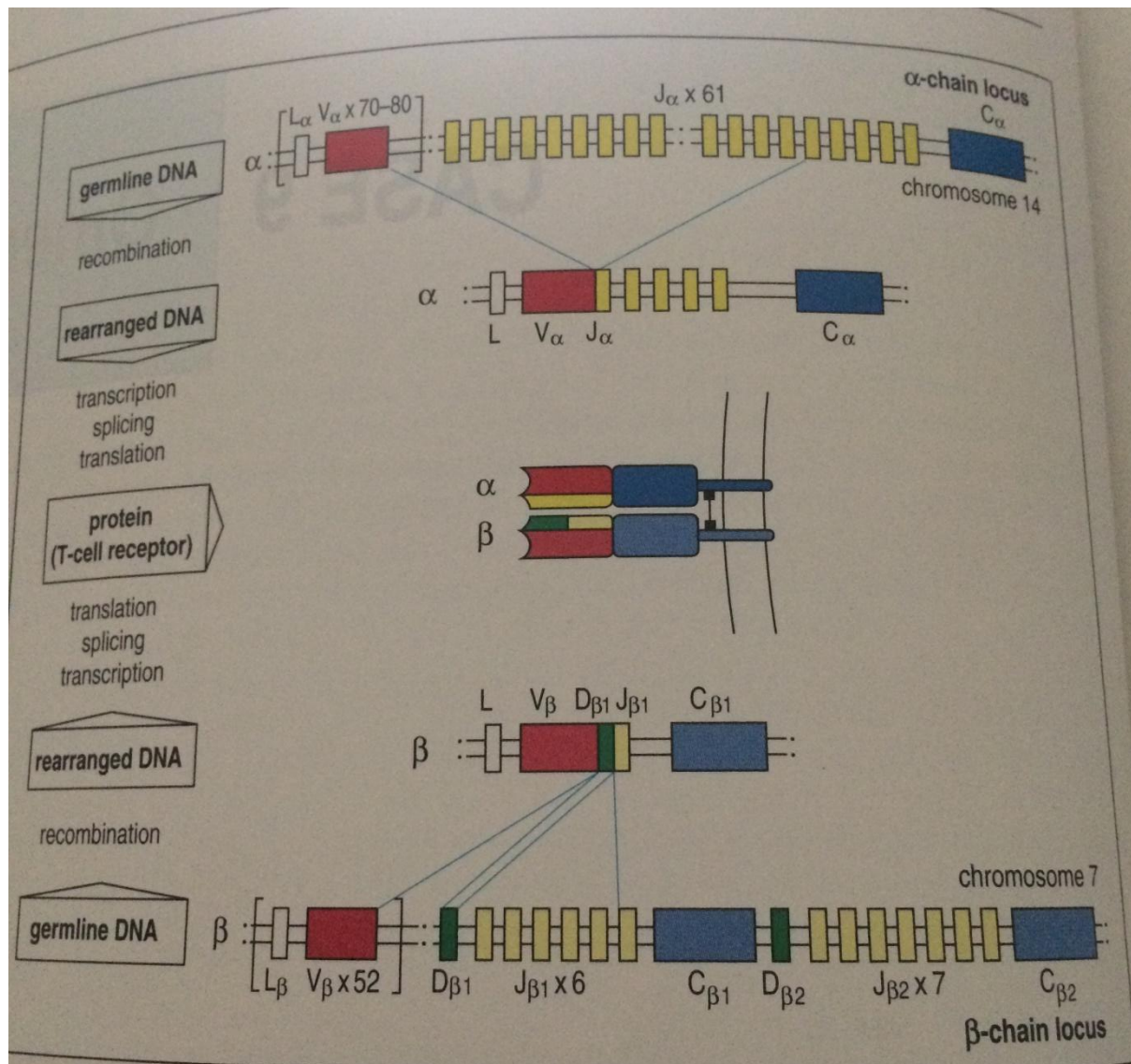
Case Study

Defect in RAG-1 or RAG-2

Recombinase activating genes (RAG-1 and RAG-2)

Total loss= SCID, partial loss= Omenn Syndrome
(Omenn due to a missense mutation)

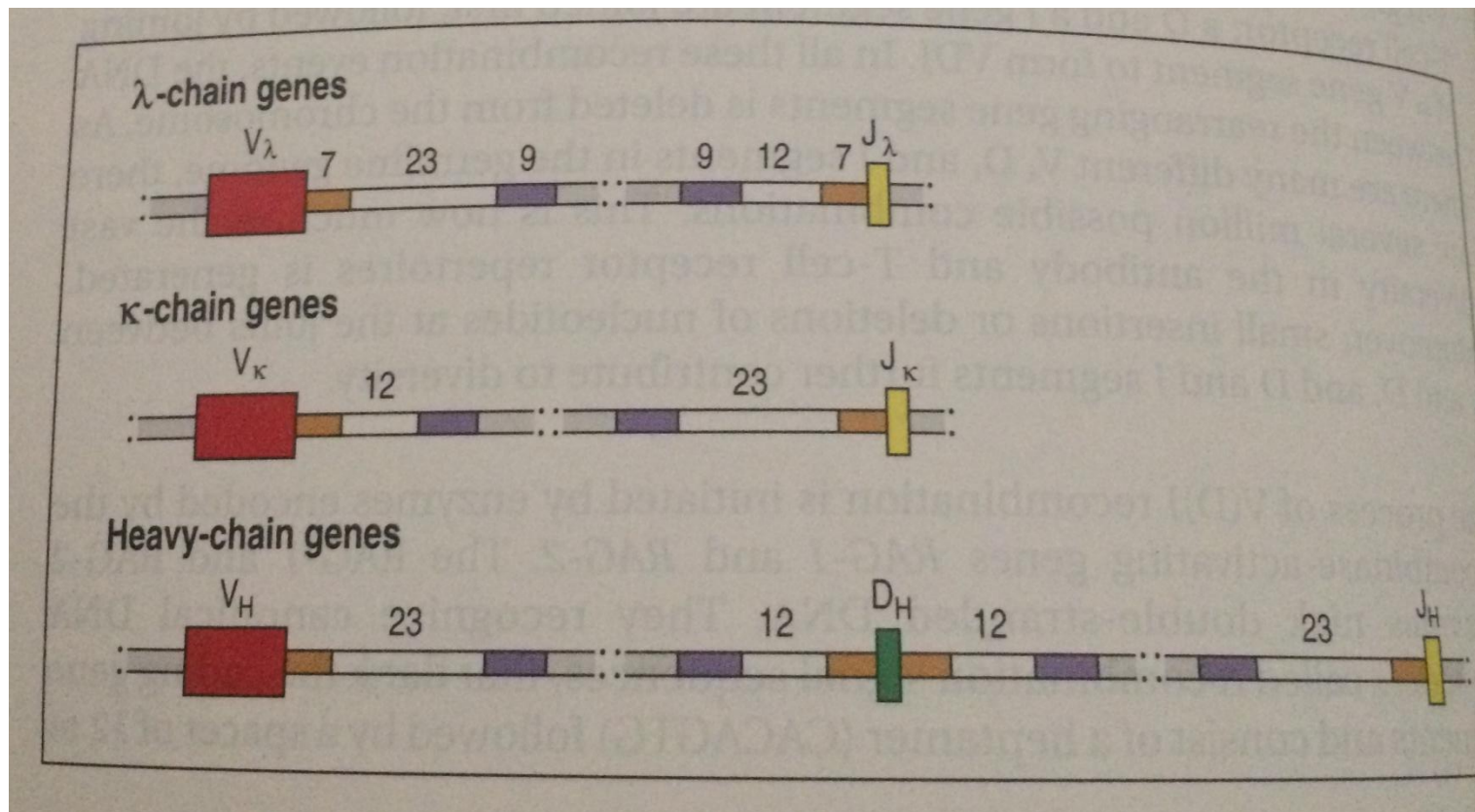
Bind to Recombination Signal Sequences (RSS) and
Nick ds-DNA.



RAG-1 and RAG-2 are involved in both Ig and TCR recombination. Hence SCID if lost.

Alpha TCR subunit is made of V and J segments only (Same as Ig light chain).

Beta subunit made of V , D , and J segments. (Same as Ig heavy chain).



Recombination signal sequences are composed of a heptamer (CACAGTG) followed by a spacer of 12 or 23 bases and then a nonamer (ACAAAAGTG)

RAG-1 binds to the nonamer, and RAG-2 to the heptamer.

Case of Ricardo Reis

Bright red rash all over the body.

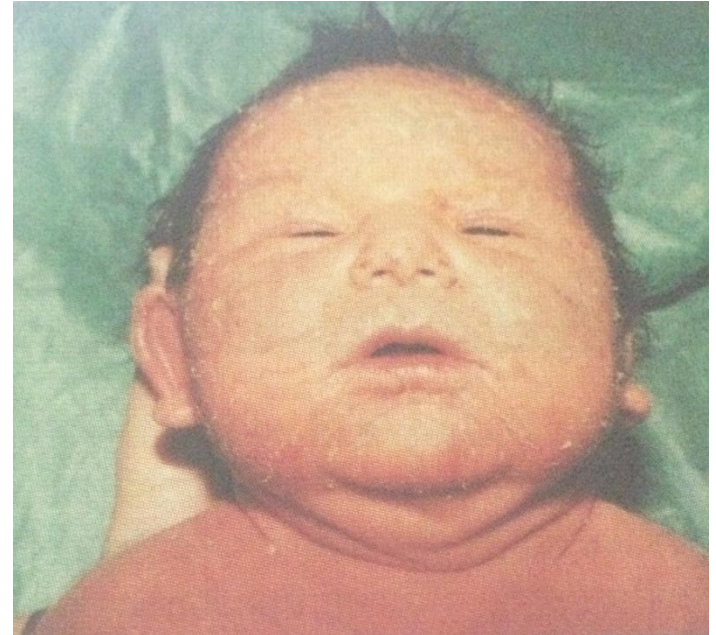
Purulent conjunctivitis

Eosinophilia (56%) and low lymphocyte count
No detectable B cells and very low T cells

Low Ig blood levels, except for IgE

Enlarged lymph nodes

Opportunistic Infections (Candida, etc..)



How do you explain high IgE and eosinophilia?

The few existing T cells have a Th2 phenotype (IL-4, IL-5 secreting)

How do you explain lymph node enlargement?

Few existing T cells are activated, and expanded within the lymph nodes.

How is RAG function assessed?

Patient and normal sequences cloned into a viral vector and inserted into fibroblasts. Substrate DNA (containing heptamers and nonamers) is added to fibroblasts. After few hours, amount of recombined DNA is measured.

What is Omenn Syndrome mode of inheritance?

Autosomal recessive

What causes the bright rash in Omenn Syndrome?

Activated T cells have homing receptors to the skin. There, they secrete chemokines that attract inflammatory cells such as monocytes and eosinophils into the skin. Perivascular inflammation= dilation of blood vessels= bright red rash.

Recommended References

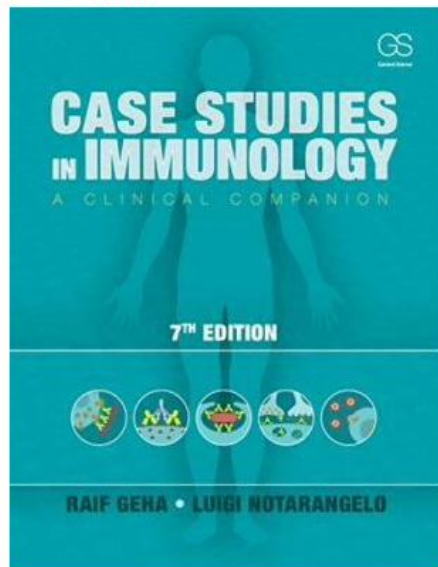
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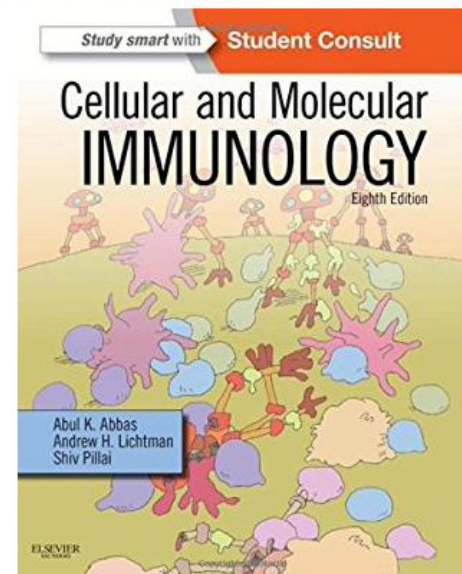
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