What happens if something goes wrong?
Immunodeficiencies Part 2 of 2

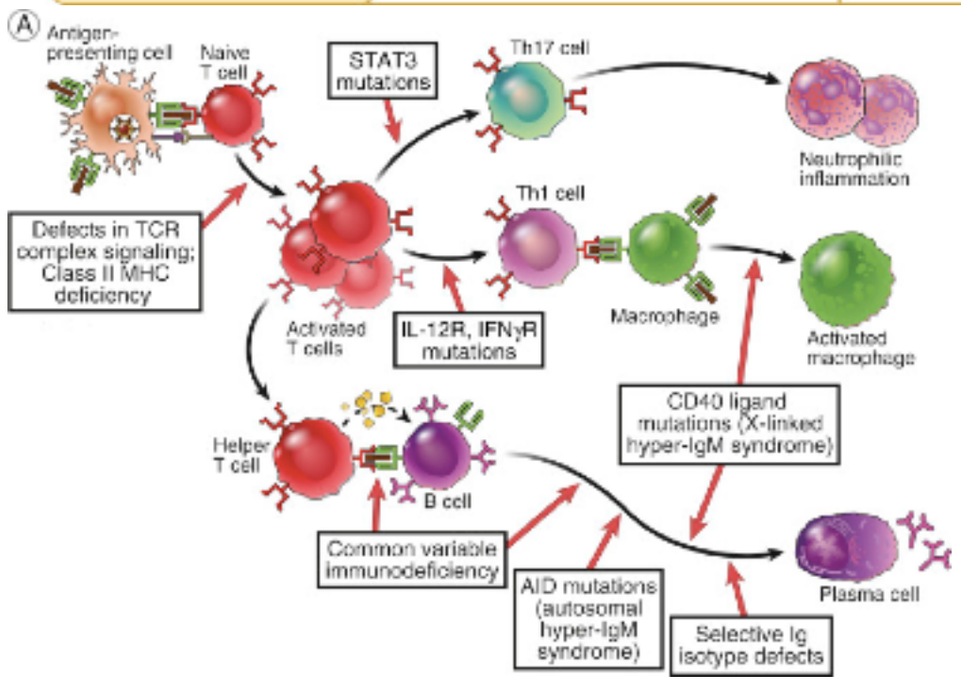
There are two big categories of immunodeficiency relevant to this case. Determining which parts of a patient's immune system are normal or abnormal can help narrow the underlying genetic cause, but also guide treatment, including prophylactic antibiotics, vaccination strategies, or determining if the patient is a candidate for a stem cell transplant. Newer treatment strategies of genome alteration may become available.

(2) Defects in Lymphocyte Activation and Function
Congenital immunodeficiencies may be caused by genetic defects in the expression of molecules required for antigen presentation to T cells, T or B lymphocyte antigen receptor signaling, helper T cell activation of B cells and macrophages, and differentiation of antibody-producing B cells. Examples include AID (Activation-induced deaminase) an enzyme which mediates class switch recombination (CSR); SAP (SLAM-associated protein) and ZAP-70 (ζ chain–associated protein of 70 kD) which are signaling molecules in T cell activation. Defects in memory B and T cells can also occur (not shown). Note that abnormalities in class II MHC expression and TCR complex signaling can cause defective T cell maturation as well as defective activation of the cells that do mature.

B

Disease	Functional Deficiencies	Mechanisms of Defect
X-linked hyper-IgM syndrome	Defects in helper T cell–dependent B cell and macrophage activation	Mutations in CD40 ligand
Common variable immunodeficiency	Reduced or no production of selective isotypes or subtypes of immunoglobulins; susceptibility to bacterial infections or no clinical problems	Mutations in receptors for B cell growth factors, costimulators
Defective class II MHC expression: the bare lymphocyte syndrome	Lack of class II MHC expression and impaired $CD4^+$ T cell activation; defective cell-mediated immunity and T cell–dependent humoral immunity	Mutations in genes encoding transcription factors required for class II MHC gene expression
Defects in T cell receptor complex expression or signaling	Decreased T cells or abnormal ratios of $CD4^+$ and $CD8^+$ subsets; decreased cell-mediated immunity	Rare cases due to mutations or deletions in genes encoding CD3 proteins, ZAP-70
Defects in Th1 differentiation	Decreased T cell–mediated macrophage activation; susceptibility to infection	Rare cases due to mutations encoding the receptors for IL-12 or interferon-γ
Defects in Th17 differentiation	Decreased T cell–mediated inflammatory responses; mucocutaneous candidiasis, bacterial skin abscesses	Rare cases due to mutations in genes encoding STAT3, IL-17, IL-17R
X-linked lymphoproliferative syndrome	Uncontrolled EBV-induced B cell proliferation and CTL activation; defective NK cell and CTL function and antibody responses	Mutations in gene encoding SAP (an adaptor protein involved in signaling in lymphocytes)

A



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