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TD03 correction – Molecular & Cellular Immunology

Exercise 1:

1. **Dendritic Cells** are most likely critically affected. They are the primary APCs responsible for activating naïve T cells in the lymph nodes, and this activation absolutely requires both antigen/MHC presentation and co-stimulation.
2. Without the **"Signal 2"** provided by co-stimulatory molecules like CD80/CD86 binding to CD28 on the T cell, the T cell does not become fully activated. Instead of proliferating and differentiating into effector cells, it may become **anergic (unresponsive)** or undergo apoptosis, leading to a poor adaptive immune response.
3. **Macrophages and B lymphocytes** could still present the bacterial antigens.
    - **Macrophages** are tissue-resident and do not typically migrate to lymph nodes to prime *naïve* T cells. They are more important for re-activating memory or effector T cells at the site of infection.
    - **B lymphocytes** require their specific BCR to recognize and internalize the antigen efficiently. They would only be effective if their BCR matches an antigen from this specific bacterium. They also often require initial help from T cells (which are not being activated) for their own full activation.

Exercise 2:

1. The defective process is the **migration of mature dendritic cells from the peripheral tissue (skin) to the regional lymph nodes**.
2. Naïve T cells circulate through lymph nodes, not peripheral tissues. If dendritic cells don't bring the antigen to the lymph nodes, the naïve T cells specific for that pathogen will never encounter it and will not be activated. This leaves the patient reliant on the slower and less specific innate immune response.
3. The **CCR7** receptor is critical for dendritic cells to follow the chemokine gradient (CCL19/CCL21) to the lymph nodes. A defect in this pathway would cause the described symptom.
4. Immunological memory depends on the initial activation of naïve T cells to create memory T cells. Without dendritic cell migration, this primary T-cell activation never happens, so no pathogen-specific memory T cells are generated, leading to recurrent infections.

Exercise 3:

1. The adjuvant acts as a **"danger signal."** It activates dendritic cells via Pattern Recognition Receptors (PRRs), triggering their maturation, which includes upregulation of MHC and co-stimulatory molecules (CD80/86).
2. Without CD80/CD86, the T cell only receives "Signal 1" (antigen/MHC). This is insufficient for activation and leads to **T-cell anergy** (a state of functional unresponsiveness) or apoptosis. The adaptive immune response is not initiated.
3. **Signal 1:** Antigen presented by MHC to the T-cell receptor (TCR). **Signal 2:** Co-stimulation (e.g., CD80/86 on APC binding to CD28 on T cell).
4. They would have severe problems with **new infections**. The primary immune response, which requires naïve T cell activation, would be defective. Their memory response to *previous* infections might be intact if memory T cells were generated before the defect manifested.

Exercise 4:

1. The patient is missing the **antigen-presenting function of B cells**.
2. B cells are highly efficient at concentrating low doses of antigen via their specific BCR and presenting them to helper T cells. This "antigen focus" provides sustained stimulation to T cells, amplifying their response. Without B cells, T-cell activation relies solely on dendritic cells and macrophages, which can lead to a slower, weaker response.
3. The robust T-cell help generated through B-cell presentation is crucial for the development of long-lived memory T cells and memory B cells. Without this efficient interaction, the memory pool may be smaller and less functional.
4. **Dendritic cells** capture antigens broadly (e.g., through phagocytosis). **B cells** capture antigens **specifically** via their BCR. This allows B cells to efficiently present *specific* antigens even when they are at very low concentrations in the body during an ongoing infection, which helps sustain the T-cell response.

Exercise 5:

1. **Disease A:** M1 (pro-inflammatory). **Disease B:** M2 (anti-inflammatory, pro-repair).
2. Receptors like **Toll-like Receptors (TLRs)** or **Interferon-gamma receptor (IFN-γR)** could be involved in driving the M1 pro-inflammatory polarization.
3. TAMs typically have **poor antigen-presenting and co-stimulatory capacity**. They often fail to provide strong "Signal 2," which can inactivate T cells that infiltrate the tumor (leading to T-cell anergy). This creates an immunosuppressive microenvironment that allows the tumor to evade the immune system.
4. The normal role of M2 macrophages is to **resolve inflammation and repair tissue** after an infection or injury. In cancer, the tumor microenvironment "hijacks" this repair program, using M2 macrophages to promote tumor growth (angiogenesis) and suppress anti-tumor immunity.