**The People's Democratic Republic of Algeria**
**Ministry of Higher Education and Scientific Research**
**University Center of Mila**
**Faculty of Natural and Life Sciences**
**Department of Biological and Agronomic Sciences**

**TD 03 – Molecular & Cellular Immunology**

## Exercise 1:

A patient has a persistent bacterial infection. Lab tests show a poor CD4+ T helper cell response, even though the T cells themselves are functional. Investigations reveal a rare genetic disorder that impairs the expression of co-stimulatory molecules on certain immune cells.

**Questions:**

1. Which type of immune cell is most likely affected by this disorder in the context of initiating a T-cell response?
2. Explain why the lack of co-stimulatory molecules would lead to a poor T-cell response.
3. Besides the defective cells, which other APCs could still present the bacterial antigens, and what might be a limitation of their response in this scenario?

## Exercise 2:

A 45-year-old man presents with multiple, persistent, and non-healing skin lesions on his arms and legs. He reports that minor cuts and scratches take months to heal and often become infected. A blood test reveals a normal number of T and B lymphocytes. However, a skin biopsy shows a significant lack of dendritic cell migration from the skin to the regional lymph nodes.

**Questions:**

1. Based on the biopsy finding, which specific process in the immune response is likely defective?
2. Explain the consequence of this defect. Why are this patient's T cells not being activated effectively despite being present in normal numbers?
3. Which receptor or signaling pathway, mentioned in the document, might be mutated or deficient in this patient's dendritic cells?
4. How would this defect specifically impact the development of **immunological memory** to the pathogens entering through his skin?

## Exercise 3:

A team of researchers is testing a new protein-based vaccine against a respiratory virus. In mouse models, the vaccine leads to a strong antibody response when injected with an **adjuvant** (an additive that boosts immunity). However, when the adjuvant is omitted, the vaccine fails to generate protective immunity. Further experiments show that without the adjuvant, dendritic cells in the muscle tissue do not upregulate co-stimulatory molecules like CD80/CD86.

**Questions:**

1. What is the primary role of the adjuvant in this context, based on its effect on dendritic cells?
2. Explain why the lack of CD80/CD86 upregulation leads to vaccine failure, even though the dendritic cells still present the vaccine antigen via MHC-II.
3. This scenario illustrates the "two-signal model" of T-cell activation. Identify "Signal 1" and "Signal 2" in this model.
4. If a patient had a genetic defect affecting CD80/CD86 expression, would you expect them to have problems fighting off *new* infections, *recurring* infections, or both? Justify your answer.

## Exercise 4:

A patient with a rare B-cell deficiency (lacks mature B cells) is infected with a virus. The patient is able to clear the initial infection, but their doctor is concerned about two things: 1) the initial T-cell response was somewhat delayed and weaker than expected, and 2) the patient does not develop long-term immunity and gets re-infected by the same virus a year later.

**Questions:**

1. Besides antibody production, what other key APC function of B cells is missing in this patient?
2. How does this missing function explain the delayed and weaker T-cell response during the initial infection?
3. How could the lack of B cells as APCs contribute to the failure in generating robust **long-term T-cell memory**?
4. Contrast the way a dendritic cell and a B cell capture antigen for presentation. Why is the B cell's method particularly valuable during an ongoing infection?

## Exercise 5:

A researcher is studying two different diseases.

- **Disease A:** A patient with rheumatoid arthritis has chronically inflamed joints. Analysis of the synovial fluid shows a high proportion of macrophages producing pro-inflammatory cytokines like TNF-α.
- **Disease B:** A patient with a large, progressive tumor has macrophages within the tumor mass that are producing growth factors and anti-inflammatory cytokines, which help suppress the local immune response.

**Questions:**

1. Identify the likely polarization state (M1 or M2) of the macrophages in **Disease A** and **Disease B**.
2. For **Disease A**, what is one receptor on macrophages that might be involved in their pro-inflammatory activation?
3. For **Disease B** (the tumor), these macrophages are often called Tumor-Associated Macrophages (TAMs). How do their APC functions (antigen presentation and co-stimulation) likely compare to a dendritic cell fighting an acute infection? How does this help the tumor survive?
4. Based on the document, what is the normal, beneficial role of M2 macrophages, and how is this role being "hijacked" in the cancer patient?