Module 2 Assignment

585.651 Immunoenginnering

1. Complete the Excel Worksheet titled “Worksheet 2 – Immune Cell Type”. (10 points)

2. Research more about one of the following communication strategies that immune cells use to communicate with each other: (40 points)
    a) Cytokine/Chemokine
    b) Major histocompatibility complex (MHC)
    c) Complement

    As you research, answer briefly (3-5 bullet points for each):

Major histocompatibility complex (MHC)

a) What cells participate in this communication (i.e. what cells produce/receive)?

1. Killer T cells can inspect class I molecules onto the surface of the cell to discover the cell has been infected and destroy it.
2. Certain antigen presenting cells (APCs), such as macrophages when they phagocyte viruses or bacteria, load fragment of viral proteins onto class II MHC molecules for display and to inform helper T cells that the infection is happening outside of cells.
3. Natural killer cells (NKs) use low class I MHC protein expression to destroy virus-infected cells, bacteria, parasites or fungi.
4. Activated Dendritic cells (DCs) class II MHC molecules are loaded with antigens to be displayed at the surface of the cell. In addition, when a DC is infected, it upregulates its class I MHC molecules to display viral proteins.
5. Once activated B cells levels of class II MHC increase allowing B cell to act as antigen presenting cell to CD4+ T cells.

b) What role does this communication play in the immune response?

1) Ability to detect pathogens: the class I MHC molecules display a sample of all the proteins being made inside a cell. Class II molecules display proteins created outside of the cells.
2) Response to inflammation: antigen presentation result in T cell activation which then kill invading pathogens or viruses.
3) MHC genes enforce “tissue compatibility” (histocompability): which ultimately determine the success of organ transplantation. Killer T cells, sensitive to MHC molecules, will eliminate foreign cells, particularly those in blood vessel, cutting off blood supply to the transplanted organ.

c) What is the consequence of this communication going awry (i.e. what disease states are associated with ineffective communication)?

1) MHC deficiencies can impair the immune system's ability to recognize and eliminate cancer cells (https://www.frontiersin.org/articles/10.3389/fimmu.2021.636568/full).
2) People with Bare Lymphocyte Syndrome (BLS) which is caused by mutations in class II MHC genes (BLS II) lack all immune protection from bacteria, viruses or fungi.
3) Autoimmune diseases: defects in MHC molecules can lead to diseases such as Type 1 Diabetes, multiple sclerosis, and rheumatoid arthritis (https://www.frontiersin.org/articles/10.3389/fimmu.2013.00321/full#:~:text=Major%20histocompatibility%20complex%20(MHC)%20genes,others%20(1%E2%80%933).)

d) Are there any therapies targeting this communication?

1) Tumor-specific antigens or neoantigens can be presented by MHC molecules of cancer cells and neoantigen-based cancer vaccines are being developed to stimulate the patient's immune system to recognize and target those [1].
2) As of 2019, the only cure for BLS; is allogeneic hematopoietic cell transplantation (HCT) or Ig replacement therapy (https://primaryimmune.org/understanding-primary-immunodeficiency/types-of-pi/bare-lymphocyte-syndrome-type-1-and-2).
3) Diabetes type I: A20 protein has been identified and currently under clinical trial to be injected into the donor islet cells to slow or stop the received immune system from damaging them (https://www.garvan.org.au/news-resources/news/world-first-gene-therapy-clinical-trial-for-type-1-diabetes).

Suggested Resources/reading:

- Janeway Immunobiology or other immunology textbook
- NIAID's website: https://www.niaid.nih.gov/research/immune-system-overview
- British Society for Immunology website: https://www.immunology.org/public-information/bitesized-immunology
- Any published literature: Search key terms in Google Scholar
- You can also use online sources (make sure to cite all sources used)

3. Making connections between vaccine design and the immune system response. (30 points)

a) What is an adjuvant and what does an adjuvant mimic?

The purpose of adjuvant is to trigger the innate immune response that provide a stimulus to the dendritic cells (DCs); they also deliver the antigen in an optimized form for DC. They can also act as damage-associated molecular patterns (DAMPs) or pathogen-associated molecular patterns (PAMPs), which can interact with pattern-recognition receptors (PRRs) on antigen presenting cells (APCs) and lead to the activation and maturation of APCs. When adding adjuvants to the vaccine, mature APCs have better ability to present antigens and express high levels of co-stimulatory signals and cytokines [2].

b) How do adjuvants interact with the immune system?

Certain adjuvants can cause cell and tissue damage through chemical irritation or direct toxic effects, leading to the release of damage-associated molecular patterns (DAMPs). Other

adjuvants contain microbial products, which similarly instigate the release of pathogen-associated molecular patterns (PAMPs). These, in turn, activate PRRs on APCs or DCs subsequently initiating the release of cytokines. These cytokines promote helper T cell responses and activate both B and T cells. Additionally, some adjuvants consist in particles coated with antigen, cytokines and costimulatory molecules, designed to optimize their uptake and processing by APCs [2].

c) What are some examples of adjuvants?

Aluminum: has been used in vaccines since the 1930s.

AS01$_B$: is an adjuvant suspension used with the antigen component of Shingrix vaccine. It is a component of vaccines including malaria and HIV vaccines.

MatrixM: is made of saponins derived from the soapbark tree and used in the Novavax COVID-19 vaccine.

d) Why do we need adjuvants in vaccines? In what cases do vaccines not require adjuvants and why?

We have established that adjuvants helps some vaccines to create a stronger immune response. Some vaccines like conjugated meningococcal vaccines do not need adjuvants because the vaccines themselves elicit a strong immune response. Certain healthy populations, have fully functional immune system and can build a strong response to the vaccine antigens without the need of an adjuvant.

Suggested Resources/reading:

- The NIH's website which is part of your reading assignment will be a good resource: https://www.niaid.nih.gov/research/vaccines

4. Develop a multiple-choice question to test someone's understanding of the immune system. Provide the correct answer and the rationale for why the other answers are not correct. (10 points)

1) Which cells are not part of the immune system?
a) Mast cells
b) Macrophages
c) Neutrophils
d) Natural killers
e) Dendritic cells
f) Myocytes

f: Myocytes are muscle cells and ae involved in the contraction of the muscle.

2) Which T cells are loaded with both class I or II MHC
a) Dendritic cell (DC)

b) CD4 T cell
c) CD8 T cell

a: DC can express both class I and class II MHC proteins therefore they can activate both helper T cells (CD4+ T cells) and cytotoxic T cells (CD8+). CD4 receptor on a helper T cells can only bind to class II MHC and CD8 receptor on a cytotoxic T cell can only bind to MHC-1.

3) Which of the following cell types of the innate immune system does not perform phagocytosis?
a) Neutrophils
b) Basophils
c) Macrophages
d) Cytotoxic T cells

d: CD4 + T cells are not phagocytic, but rather release cytokines which help to activate CD8+ T cell, B cells and macrophages.

4) Which of the following options is not a mechanism by which an antibody can protect against a pathogen?
a) Defense against viruses
b) Co-stimulation of T cells
c) Opsonization
d) Complement activation

b: Co-stimulation of T cells
T cell activation not only requires the recognition of an MHC complex by the T cell receptor (TCR) but also additional signals from co-stimulatory molecules.

Antibodies can bind directly to viruses, bacteria preventing them from attacking or entering host cells. Antibodies can initiate the complement cascade that leads to the lysis of pathogens, further opsonization, which involves the binding of antibodies to the surface of a pathogen, tagging them for destruction by macrophages or neutrophils.

5) Which of the following events do not occur during immune response?
a) Cytokine secretion
b) Chemokine secretion
c) Recruitment of innate immune cells
d) Constriction of blood vessels

d: constriction of blood vessels could happen, but it is not part of the inflammatory response. During inflammation, cytokines are released to recruit immune cell to the site of infection. Cytokines, such as TNF, can kill tumor cells and virus-infected cells. The movement of immune cells through a lymph node is orchestrated by a subset of cytokines, the chemokines.

6) Which cells are part of the adaptative immune system?
a) T cells
b) B cells
c) Macrophages
d) Dendritic cells
e) Only a and b

Only a and b, macrophages and dendritic cells are part of the innate immunity system.

7) In which part of the body B cells are created in adults?
a) Thymus
b) Spleen
c) Liver
d) Lymph nodes
e) Bone marrow

e: B cells are created in the bone marrow.

8) Which mature B cells can become?
a) Plasma cells
b) Memory cells
c) Hematopoietic stem cells (HSC)

a and b: HSCs can develop into B cells not the reverse.

9) Typical time after infection to the start of the adaptive immune response:
a) Minutes
b) Hours
c) Days

b and c: Hours or days: it takes some time for the lymphocytes to have differentiated into antigen specific T and B cell, to proliferate and differentiate into cytotoxic lymphocytes cells (CTL: NK, CD4+ and CD8+ cells).

10) Which of the following is not one of the antigen-presenting cell types:
a) Dendritic cells
b) Lymphocytes
c) Natural killer cells
d) Macrophages

c: Natural killer cells secrete cytotoxic chemical but are not part of antigen-presenting cell types (APCs)

[1] N. Biswas, S. Chakrabarti, V. Padul, L. D. Jones, and S. Ashili, "Designing neoantigen cancer vaccines, trials, and outcomes," *Front. Immunol.*, vol. 14, p. 1105420, 2023, doi: 10.3389/fimmu.2023.1105420

[2] T. Zhao *et al.*, "Vaccine adjuvants: mechanisms and platforms," *Signal Transduct. Target. Ther.*, vol. 8, no. 1, p. 283, 2023, doi: 10.1038/s41392-023-01557-7

[3]: adjuvants and vaccines CDC reference: https://www.cdc.gov/vaccinesafety/concerns/adjuvants.html#alum