Problem Set 1 – Immunology – Spring 2026

Do not use AI in preparing your answers (e.g., ChatGPT or any similar LLM).

1. Based on Dr. Vinod Balachandran's lecture (submitted by Linsey Zhang):

Tumor Immunology Problem Set

Extra reading (recommended):
A neoantigen vaccine generates antitumour immunity in renal cell carcinoma. PMID: 39910301

In the lecture, we discussed the use of mRNA cancer vaccines for pancreatic cancer and reviewed the use of lipid nanoparticles (LNPs) for delivery. Currently, cancer vaccines are being tested across multiple cancer types, ranging from immunologically "cold" to "hot" tumors.

Please answer Question 1 and choose **one** of Questions 2 or 3 to answer.

1) Although we primarily discussed mRNA vaccines in the lecture, the field of cancer vaccines is broadly divided into two groups: mRNA-based vaccines and peptide-based vaccines. Based on the lecture discussions and the extra reading provided, briefly discuss the rationale behind each strategy, as well as their associated delivery modes (e.g., IM, IV). Why might one strategy be preferred over another for certain cancer types? What are the differences in post-vaccination immunophenotypes?

2) Based on the 2023 paper discussed in the lecture, not all patients respond to vaccines. Furthermore, among responders, some exhibit polytopic responses while others exhibit monotopic responses. Although monotopic responses can provide some level of protection, the field generally believes that responses against multiple neoantigens lead to stronger protection. Design an experiment to test whether monotopic or polytopic responses provide better protection against tumor recurrence (you may use pancreatic cancer as a model, but you are free to use any cancer model with which you are familiar). Be sure to include controls, expected results, and interpretations.

3) Based on current knowledge of infectious disease vaccines, what improvements could be made to current cancer vaccines to enhance immune responses? Design an experiment to test your hypothesis and list the expected results. What do you think are the biggest limitations in translating knowledge from infectious disease vaccines to cancer vaccines?

Problem Set 1 – Immunology – Spring 2026

2. From Dr. Simon Grassman:

Type-I interferon and interleukin(IL-)12 both can activate STAT4, however type-I interferon mostly signals through STAT1/STAT2/IRF9. In today's paper we saw that antigen signaling modifies STAT4 signaling to drive adaptive programming of NK cells and $CD8^+$ T cells. An open question is if STAT4 activated by type-I interferon has the same effect.

Design a project to determine whether type I interferon and IL-12 regulate cytotoxic lymphocyte differentiation redundantly or through distinct mechanisms.

Specify:

(i) the model systems (*in vitro* and/or *in vivo*)

(ii) the perturbations and controls

(iii) the readouts of differentiation and function

(iv) the results you would expect under a redundant vs distinct model.

Problem Set 1 – Immunology – Spring 2026

3. Based on Dr. Alan Hanash's lecture (Submitted by Andrea Lang Goldgewict):

Protein X is expressed by T cells and involved in basic T cell biology. Data from your lab shows that it is upregulated upon T cell activation and that it is expressed by donor T cells after allogeneic bone marrow transplantation. Congratulations! your PI has assigned you to take over this exciting project. There are several questions that you must answer before beginning your experiments.

(a) What are two T-cell-dependent aspects of allogeneic bone marrow transplant biology that could be impacted by protein X. Describe them each in 2-3 sentences.

(b) Design an experiment to test the effects of protein X on one of the aspects you discussed above. Make sure to detail your experimental model, controls, expected results, and how you would interpret them. (maximum 1/2 page).

Problem Set 1 – Immunology – Spring 2026

4. From Dr Luc Morris:

Describe the concept of immune equilibrium as it relates to surveillance of cancer, and provide an example of a mechanism by which immune equilibrium is carried out. Design an experiment to identify the immune cell population(s) involved in equilibrium of a type of cancer you are studying. The experiment could be one conduced in a model system, or an analysis of cancer in human patients.

Problem Set 1 – Immunology – Spring 2026

5. From Brianna Naizir's lecture:

Outline the steps of the immune response example from **the lecture slides**: from breach of anatomical barriers to activation of the immune system. Provide a timeline and be specific- name the cell types that are engaged and interact, timing and location of the response, and mechanisms of immune defense against pathogen (including receptors, effector molecules, etc).