Instructions: This exam consists of 22 questions on 11 pages for a total of 200 points. On questions with choices, all of your attempts will be graded and you will receive the best score. Place your name on each page.

1. (10 pts) Compare and contrast central versus peripheral tolerance, both in terms of location and the general events that occur to generate tolerance to self-antigens.

2. (10 pts) Please do one of the following choices.
   - **Choice A:** How do T_{reg} cells prevent autoimmune diseases.
   - **Choice B:** Briefly exchange why food allergies are relatively uncommon, what immunological mechanisms are at play to reduce the response to antigens in our food?
3. (10 pts) Pick **two** of the following diseases and state which type of hypersensitivity is responsible for the immune response. Briefly justify your answer with reference to the nature of the antigen and the immune response (Note: You may complete Q21 first. Feel free to reference that table in your answer below.)

   i. Rheumatic fever
   ii. Graves’ Disease
   iii. Myasthenia gravis
   iv. Lupus
   v. Diabetes – type I
   vi. Multiple sclerosis
   vii. Sympathetic ophthalmia
   viii. Serum sickness
   ix. Penicillin allergy

4. (8 pts) A transplant patient receives a new kidney, and organ rejection begins almost immediately.
   i) What mistake did the transplant team make?
   ii) What immunological processes are occurring to cause rejection of the kidney?
5. (12 pts) A second kidney transplant is attempted and the kidney is rejected after about two weeks.
   i) Briefly describe the most likely rejection mechanism, in particular how the host’s immune system became sensitized to the transplanted organ.
   ii) The transplant team neglected to run a simple test to determine if rejection was likely. What test was that and how would the test have informed the transplant team as to the success of the transplant.

6. (8 pts) A third transplant is attempted, and this time the patient was treated with:
   i) Cyclosporine,
   ii) An anti-IL2Rα antibody,
   iii) An injection of the donor’s bone marrow.

   The kidney is not rejected. Briefly discuss how two of the above treatments prevented rejection of the kidney.
7. (5 pts) The transplant team carefully monitors the health of the transplanted kidney. What methods could they use to do so and what are the comparative advantageous of one method over another?

8. (4 pts) The following molecules are involved in B-cell/T-cell signaling: CD40, CD40L, b7, CD28. How would the loss of any one of these, due to a genetic deficiency, affect the ability of someone to respond to pathogens that enter via the mucosal membrane?
9. (8 pts) Discuss the interplay between the innate and the acquired system using an example. What innate processes are essential for the acquired response and how can the acquired response supplement, or aid, the innate response?

10. (12 pts) Differences in the diversity and specificity of the B-cell receptor (BCR), MHC, and the T-cell receptor (TCR) are important in the normal function of the immune system.
   i) Briefly describe how diversity is generated for BCR or TCR and MHC (i.e. pick B or T, and do MHC). Comment on whether the diversity is at the level of a single cell, within a single organism, or the population.
   ii) Briefly describe the specificity of these proteins and how the specificity (or lack of) is an essential property of the immune system.
11. (4 pts) Discuss one genetic deficiency that could cause a severe combined immunodeficiency (SCID).

12. (6 pts) What enzymes in the HIV lifecycle are currently inhibited by anti-HIV drugs. What are the roles of these enzymes in the HIV lifecycle?

13. (6 pts) Please do one of the following choices:
   - Choice A: Briefly describe how you might make an HIV vaccine using measles virus.
   - Choice B: Certain HIV resistant individuals are missing a protein. What is this protein, and why are they resistant to HIV?
   - Choice C: How did biochemical studies confirm the major features of the TCR-MHC interaction as observed in the crystal structure?
   - Choice D: How do class I and class II MHCs differ in their ability to present peptides.
   - Choice E: Discuss one application of “engineered” antibodies in disease treatment.
14. (14 pts) The Complement System. Please answer all of the following.
   i. What functions does the complement system play in innate immunity? Briefly describe each of these functions (precisely mention the effector, how it is generated? how it mediates its function?)
   ii. How does the complement system directly participate in eliminating viral particles and virally infected cells?
   iii. Describe the effects of a genetic disorder that perturbs the expression of the C3 complement subunit

15. (5 pts) What are the differences between active and passive immunization? Give an example for each.

16. (6 pts) The Gut-Associated Lymphoid Tissue (GALT) is the digestive tract immune system. Describe how the GALT protects the body against ingested pathogens?
17. (10 pts) The flu virus evades the immune system by undergoing antigenic shift and antigenic drift. Describe each of these immune evasion mechanisms and clearly state the cause of each one.

18. (10 pts) Answer two questions of your choice from the following questions.
   - **Choice A:** What causes histamine release by Mast cells? (detail your answer)
   - **Choice B:** What is histamine’s role in hypersensitivity reaction type I?
   - **Choice C:** What is an adjuvant? What is its role in a vaccine?
   - **Choice D:** Give an example of a vaccination strategy and highlight its pros and cons
19. (14 pts) Trypanosoma brucei is a protozoan parasite that infects humans. The ensuing humoral immune response is mainly raised against the parasite surface protein Variant Surface Glycoprotein (VSG). Despite the efficiency of the secreted anti-VSG antibodies in clearing out the parasite, the infection persists. Please do all of the following:

i) Describe how do the anti-VSG antibodies kill the parasite?

ii) What evasion strategy used by the trypanosome allows the infection to persist? Briefly explain the mechanism.

iii) Complete the following graph, by representing the variations of the trypanosome blood concentration after several weeks of infection (Left Y axis)

iv) Describe the presented pattern and explain its causes

v) Overlay on the same graph the levels of circulating anti-VSG antibodies (Right Y axis)
20. (6 pts) How is gene therapy used as a treatment for patients with severe combined immunodeficiency (SCID)? What could be the risks of using such therapeutic strategy?

21. (16 pts) Fill out the following comparative table.

<table>
<thead>
<tr>
<th>Hypersensitivity</th>
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<th>Type II</th>
<th>Type III</th>
<th>Type IV</th>
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22. (16 pts) The following graph depicts the variation of the HIV viral load (Right Y axis-brown curve-) in an HIV seropositive patient. Please answer all of the following questions.

i) Describe the viral load variations labeled 1 to 4 in the figure and the precise cause of each of them.

ii) Complete the graph by representing the variations of the T\text{H}^\text{CD4+} blood cell count (Left Y axis) knowing that prior to infection the patient had 800 cell/μl. Explain the variations shown by your curve.

iii) On the same graph Delineate and label the 3 stages of HIV infection leading to the patient death (you can draw lines parallel to the Y axis).

iv) Overlay, on the same graph, the curve (in dotted line) representing the variation of circulating anti-HIV antibodies since infection occurred. Then, explain the variations shown by your curve.