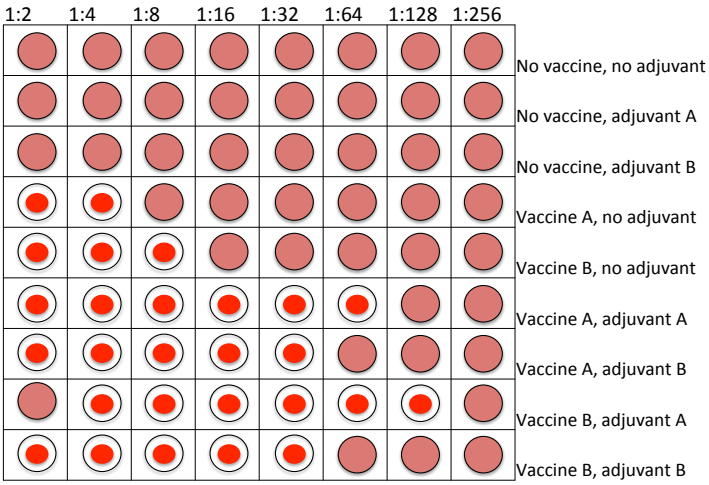
Bio 4150, Fundamentals of Immunology
Take-home Exam 6 (Final)
100 points

1. In your laboratory, you generate two new influenza vaccines and decide to test both vaccines with two possible adjuvants. You remember that IAV has a high agglutination potential, so you decide to perform a hemagglutination assay to measure the concentration of anti-IAV antibodies in the serum of laboratory mice. After immunizing mice with the indicated combinations of vaccine antigens and adjuvants, you take serum samples, dilute them, and incubate the diluted serum samples with a known titer of IAV in the presence of sheep red blood cells. A diffuse pink solution is a sign of positive agglutination, while a condensed red "button" is a sign of negative agglutination. Using the data provided here, answer the following questions and explain your thinking for each.

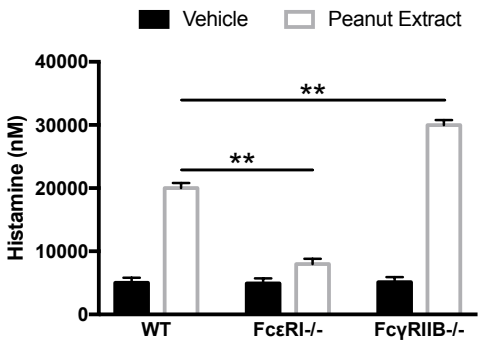


a. (**6 points)** What is the HA titer achieved by vaccines A and B in the absence of adjuvant? **(2-3 sentences)**

b. (**6 points)** Approximately how much greater is the anti-IAV antibody concentration in the sera of mice that were immunized with vaccine A in the presence of adjuvant A compared to mice that received vaccine A with no adjuvant? **(2-3 sentences)**

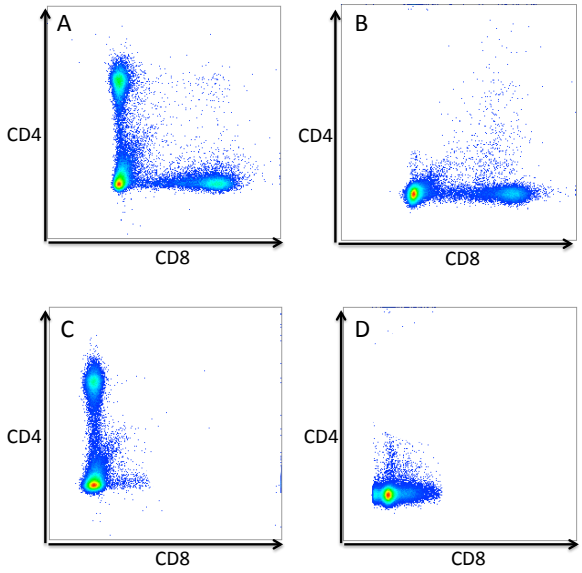
c. (**6 points)** Which adjuvant was more immunogenic overall, and what is the titer of the most immunogenic combination of vaccine and adjuvant in the experiment? **(2-3 sentences)**

2. (**14 points)** In the laboratory, you immunize a set of WT, FcεRI$^{-/-}$ and FcγRIIB$^{-/-}$ mice with peanut extract in the presence of a T_H2 polarizing adjuvant. A couple of weeks later, you orally administer peanut extract to the mice and measure the concentration of histamine in their blood. You observe the results pictured here. Explain why exposure to peanut extract results in the release of histamine in your immunized mice and how the loss of each of these Fc receptors would contribute to the observed differences in serum histamine concentration after exposure. **(5-8 sentences)**



3. (**10 points)** For a set of future experiments, you need to generate a purified population of activated dendritic cells from mice that you have previously infected with MCMV. Using either fluorescence activated or magnetic activated cell sorting, propose a strategy for isolating activated dendritic cells from the blood of your infected mice. Be sure to explain how you will specifically purify the activated dendritic cells from the unactivated dendritic cells. (**4-6 sentences)**

4. (**18 points)** In your clinic, you receive tubes of blood from 4 patients. The patients have the following health statuses:
Patient 1. Healthy control patient.
Patient 2. Patient has a severe combined immunodeficiency resulting from a genetic deficiency in RAG1.
Patient 3. Patient has bare lymphocyte syndrome resulting from genetic deficiency in MHC-II.
Patient 4. Patient has bare lymphocyte syndrome resulting from genetic deficiency in TAP.
You analyze immune cell frequencies in the blood samples via flow cytometry, yielding the attached plots. Match each patient to the flow plot that you would expect to obtain from them, based on your knowledge of their health status. Explain your thinking for each. (**8-12 sentences)**



5. (**10 points)** Mice with a genetic deficiency in the molecule CD40 experience increased susceptibility to many pathogens, but in general are more susceptible to extracellular bacteria than intracellular bacteria. Explain why loss of CD40 would differentially impact susceptibility to these two types of bacterial pathogens. **(4-6 sentences)**

6. (**10 points)** Interferon signaling is associated with the induction of the 'antiviral state.' Identify the major sources of interferon expression in the innate and adaptive immune systems and explain the major mechanisms by which they create an intracellular environment that inhibits the replication of viruses. **(4-6 sentences)**

7. (**10 points)** After experiencing kidney failure, a patient named Amy received a kidney transplant from her non-identical sibling Karen. The kidney transplant was successful and the kidney remained healthy for 12 years before beginning to show signs of chronic rejection. Once the transplanted kidney began to fail, Karen's identical twin Sonique offered to donate one of her kidneys to Amy. However, two days after transplantation of Sonique's kidney, Amy went into shock and the new kidney had to be removed. The regime of immunosuppresive drugs and antibiotics used for the second tranplant were identical to those used after Amy's first transplant. Provide a likely explanation for why Amy's body responded so differently to two genetically identical kidneys. **(4-6 sentences)**

8. (**10 points)** A promising new therapy for established tumors is the injection of autologous tumor cells that have been removed from the patient and engineered to express high levels of CD80/86. Reintroduction of these genetically modified tumor cells back into the patient may enhance antitumor immunity, resulting in cancer regression. However, this therapy may be significantly supplemented by co-treatment with a monoclonal neutralizing antibody to CTLA-4. Explain why reintroduction of CD80/86 expressing tumor cells into a patient would promote antitumor immunity, and why antibody neutralization of CTLA-4 would serve to further augment this response. **(4-6 sentences)**