

Problem Set 5:

1. Antibody diversity is partially created by the joining of random DNA segments to create the exons that code for the variable region. In this problem you will discover additional mechanisms to increase diversity.

You are sequencing the light chain gene in B-cells (i.e. after VJ joining). These two B-cells happened to use the same V and J segments when the light chain was created. You find the following protein sequences around the J-segments in two B-cells (one letter amino acid code). The gray and blue highlighted regions indicate sequences from the V-segment and the constant light exon, respectively. Suggest what might have occurred during the joining process to generate the second sequence.

Sequence 1:

-EWGGAAFQRTYESTTY
-V--|--J---|--- C-light

Sequence 2:

-EWGGAFQRTYESTTY
-V--|--J---|--- C-light

2. You are an oncologist and one of your patients is no longer responding to chemotherapy to treat their cancer. You determine the sequence of the genome of the tumor cells and find a mutation in several nuclear proteins (including p53) and a cell surface protein. Since it is easy to purify p53 you use the altered p53 to produce antibodies. You then use the antibodies to produce a bispecific antibody to activate T-cells. Will this approach help the patient?
3. What disease is the drug Blinatumomab (also known as MT103) used to treat? Briefly describe how it works to cure the patient (*please use the web and provide the appropriate citation*).

4. The R_0 value for a virus is the number of people an infected person would transmit the disease to. The R_0 values for three viral pathogens are given in the table below. Use the infectivity simulator discussed in class to answer these questions. Reminder that you must average the infectivity for 3 trials to obtain interpretable results. Use the spreadsheet on the course website to help you average and plot the infectivity rate versus vaccination rate.

Virus	R_0	Vaccination Level for Herd Immunity
Ebola	~2	
Polio	~7	
Measles	~15	

- i) Determine the level of herd immunity that is required to prevent the spread of the disease, i.e. complete the right-hand column of the table. Include a graph from the spreadsheet you used to collect your data.
- ii) How does the level of herd immunity depend on the R_0 of the virus?
5. FDA approved vaccines.
- i) Complete and submit the following table on FDA approved vaccines. The first row is done for you.
- ii) What type of vaccine is not represented in this list?
- iii) The vaccine indicated in part ii) is used to vaccinate against what type of virus?

Vaccine Name	Disease	Subunit Vac	Inactivat. virus	Live Attenuated virus	Virus Like Particle	Recomb. vaccine	RNA vaccine
1. Engerix-B	Hepatitis B	X					
2. IPOL vaccine							
3. OPV vaccine							
4. RabAvert							
5. Varivax							
6. Gardasil							
7. RotaTeq/Rotarix							
8. Fluenz							
9. Fluarix							
10. Influvac							

6. Although the HIV virus was identified in 1983 there are no effective vaccines, despite intense efforts by government and pharma. Provide an explanation as to why this is the case (Hint: you may want to research how the virus replicates and review the lecture on polymerases).