

Ideas for extra analysis to include in your report over the computer exercises (in some exercises, more information are available on the actual exercise handouts as well):

HLA-disease associations:

If you decide to write your research project report on this computer exercise, then we require that you perform the analysis suggested above, but moreover, you will need to think of and perform an extra analysis. One possibility is to study the paper by Kosmrlj et al (Nature, Vol 465, 2010, doi:10.1038/nature08997). You can focus on the following questions:

- a) For HLA-B*57, [Kosmrlj et al](#) proposes a different mechanism to explain its protective effect. Read this article and summarize for yourself what they have done, and what they conclude.

Let us define the binding fraction of an MHC molecule as the number of peptides that it binds in a proteome divided by the total number of 9mers in that proteome.

- b) Try to estimate the binding fraction of B*57 for other viruses than HIV-1 (proteome sequences of viruses are available from [EBI web page](#), 3-4 different viruses would be sufficient, if you want to have the statistics, then use more).
- c) How close are the numbers you get to the number estimated for self by [Kosmrlj et al \(Supplementary Material, Table SI, BF stands for binding fraction\)](#)? Is self the only proteome that would be presented poorly by B*5701 molecule?
- d) Study the fraction of binders from self estimated by [Kosmrlj et al \(Supplementary Material, Table SI\)](#). Compare the fractions of presented self for B*5701 and B*1801. Do you think the difference in these numbers can explain why B*5701 is protective, while B*1801 is detrimental?
- e) Study the binding motif of B*5701 using the [Sequence motifs](#) link on NetMHC page. Can the amino acid preference at the anchor positions explain the observed phenomenon? (You can find information on amino acid frequencies in the [Swissprot statistics](#), scroll down to the bottom of the page).
- f) And finally, conclude Which one of the two explanations why B*5701 is protective in HIV-1 infection do you think is more likely?

Diversity of the immune system:

If you decide to write a report on this computer practical, you can choose to write a report about the specificity of lymphocytes (Questions 1 & 2) or about the optimal number of MHC molecules (Questions 3 & 4). Read the papers that we cite above, make sure you correctly address all the answers to the questions given below, and try to add some original results.

Acute Immune responses to viruses:

If you decide to write a report on this computer practical, you could start by seeing how De Boer and Perelson (Boer and Perelson, JTB, 2013, **327**:45-87, Fig. 2) included the data from Kotturi et al. (Kotturi, et. al., JI, 2008, **181**: 2124-2133) in the modeling of the same data on the GP33 and the NP396 response to LCMV. How would the model change if memory cells were already formed during the expansion phase? Can this also explain the data, see (Kohler, B. JTB, 2007, **245**:669-676)?

Computer practica of Dr. Borghans:

If you decide to write a report on these computer practicals, you should tilt the questions to a higher level. One option is to combine two questions out of the four we have in these computer practicals, being free to combine which ever you like. For example:

- 1) TREC question of first day and TREC question of second day,
- 2) Combining what you can deduce from TREC and telomeres measurements (both first day),
- 3) Comparing techniques that claim to measure proliferation, i.e. telomeres from first day and BrdU and stable isotopes from second day.

Evolution and origin of NK cells:

If you decide to write your research project report on this computer exercise, then, you will need to think of and perform an extra analysis. One possibility is to repeat your analysis using a different protein, some candidates are mentioned in the article of Gascoyne et al. Another possibility is to focus on the question whether or not there had been any gene duplications/deletions in E4BP4 story? Are there any species that you expect to find E4BP4 but you can't?