
Reading scientific papers can be daunting, even for the seasoned scientist. Before picking up a paper it is best to have some questions in mind to focus your reading. Regardless of your questions, you may want to approach a paper in the following fashion:

- Read the abstract first, it should give you a complete summary of the paper, including important conclusions.
- Read the introduction next, a good introduction will set the stage for the results presented in the paper.
- Don’t bother with the detailed materials and methods, unless you are planning to use the techniques or repeat the experiment. In the case of Science or Nature paper, this section is often omitted and the information is presented in other sections or under references and notes.
- I look at the figures and their associated legends, to assess the actual data that the author will use to draw conclusions.
- Now read the results and discussion section. In the case of a structure paper, such as this, I usually gloss over the detailed structural information because it puts me right to sleep, unless I am interested in specific interactions.

Before reading the paper you should read the section in the text on class I MHC such that you become familiar with the structure. To gain a better appreciation for the structure I have made some Jmol pages that you can use to view the structure. If you are unfamiliar with Jmol, there is a tutorial at: https://www.andrew.cmu.edu/user/rule/bc_oli/jmol/jmol_tutorial.html

Jmol images of Class I and a comparison of Class I and Class II MHC are found at: https://www.andrew.cmu.edu/user/rule/jmol/mhc1.html & https://www.andrew.cmu.edu/user/rule/jmol/mhc1and2.html, respectively.

Questions that you should answer while reading the paper are listed below:

1. Why were initial attempts to visualize the MHCI-peptide complex unsuccessful?
2. What are the sequence differences between the two peptides?
3. What are the sequence similarities between the two peptides?
4. How does the conformation of the two bound peptides differ?
5. Are the peptides loosely bound in the cleft or deeply buried?
6. Can you explain the nM binding affinity based on the number of interactions (see Table 3 and 4). You can estimate the free energy of binding from the interactions, assume 1 H-bond = 1 kJ/mol, and one van der Waals contact = 0.5 kJ/mol. The free energy can be converted to $K_{EQ}$ using $\Delta G^o = -RT \ln K_{EQ}$; assume T=300K. A 1 nM binding affinity ($K_D$) is the same as $K_{EQ}=10^9$ M$^{-1}$. This is a “back-of-the-envelop” calculation, so don’t worry about counting all the interactions.
7. Are the MHC I-peptide interactions specific for sidechains of the bound peptide or not?
   - Are there many specific interactions between the MHC and the sidechains of the bound peptide, or are the interactions mostly with the mainchain atoms of the peptide (see Table 3 and 4)?
   - In what way are the peptide-MHC interactions dependent on the secondary structure of the peptide?
   - What does the term ‘anchor residue’ mean?
8. What structural features limit the length of the peptide that can be bound to class I MHC?

Please submit a short report that answers the above questions. As a guideline, 2-4 sentences/question should be adequate. Please answer each question separately. For those of you with artistic yearnings (and talent), a simple labeled cartoon of the peptide-MHC complex that answers one or more of the above questions would be an acceptable answer for those questions.