This problem set is to be done on your own. It will allow you to become familiar with looking at structure, thinking about important interatom distances and using BLAST and Clustal W programs as starting places for thinking about structure and function.

1. The structures of OMP decarboxylase have been solved from four different organisms in the apo form and in the presence of UMP, 6-hydroxyuridine-5'-monophosphate and 6-azaUMP. Pull up the sequences of the *S. cerevisiae*, *B. subtilis* and *Methanobacterium thermoautotrophicum* OMP decarboxylases. Submit the *B. subtilis* enzyme sequence to a BLAST search and the three sequences to Clustal W alignment.
   
   i. What is the percent sequence identity between *B. subtilis* and *M. thermoautotrophicum* and *B. subtilis* and *S. cerevisiae* OMP decarboxylase?

   ii. Show your Clustal W alignment. How many residues are absolutely conserved? What are the residues? Residues that are absolutely conserved usually play a very important role in catalysis or structure. Aligning OMP DC sequences from very diverse sources provides the most insight into important residues. Once you have mapped the structure of the active site of OMP DC (see questions 3 and 4), you should be able to show that the residues that you have identified as conserved by sequence alignment are also found in the active site.

2. Pull up the structure of OMP DC from *M. thermoautotrophicum* 1LOR. It contains a BMP analog bound in the active site. Also pull up the structure of the *B. subtilis* OMP DC. Make a topology diagram of the *B. subtilis* protein. Does it appear to be structurally homologous to the *M. thermoautotrophicum* protein?

3. Look at the structure of the *M. thermoautotrophicum* enzyme with BMP. Draw a flat diagram that includes a structure of the inhibitor and all of the amino acid residues in the vicinity of the inhibitor that could be interesting in terms of binding of the substrate or catalysis. Indicate the distances of these residues from the inhibitor. To think about mechanism, look at the handout given in class for mechanisms that have been considered for this decarboxylation reaction.

4. Repeat the same exercise for the *B. subtilis* enzyme.

5. Compare the two structures and the information from the sequence alignment. What does this comparison tell you?

6. Does this structural data eliminate any of the mechanistic options given in class from consideration? Which one(s) and why?