Molecular Modeling: Assignment V

1) Valine 523.B selected.

2) Image of ligand in mutated COX enzyme.

3) COX-2 AutoDock Vina

[Image of AutoDock Vina results for COX-2]

3) COX-1 AutoDock Vina

[Image of AutoDock Vina results for COX-1]

The binding energies in the COX-2 active site are larger than the binding energies for the COX-1 binding site. The more energy released upon binding, the more spontaneous the reaction will be. The more negative the binding energy, the more stable the product so from my autodock vina results I would predict that my inhibitor is not specific to a single version of the enzyme and it might actually interact better with the COX-2 enzyme than the COX-1 enzyme.
4) If I made my ligand bigger it would most likely react with COX-2 better than COX-1 because COX-2 has a valine substituted for an isoleucine at the 523 location. Isoleucine is a larger amino acid than valine and so if I increased the size of my amino acid it would be able to fit better with the COX-2 enzyme than the COX-1 enzyme. Isoleucine and Valine are still very similar in character, non-polar and hydrophobic.

5) Residue 355.B is the catalytic residue which is tyrosine. If I were to mutate the COX enzyme without changing the catalytic activity of the enzyme I would change a residue other than tryptophan 355. For example I could change valine 349.B to leucine without changing the catalytic activity of the enzyme. This mutation would change the steric of the reaction just like the substitution of valine for isoleucine did. I would go to tools → general controls → command bar, and type in swapaa leu: 349. After hitting enter the valine 349.B of the original enzyme would be mutated to leucine 349.B.

Y, Tyrosine 355.B is the catalytic residue of 1PTH.