In-class exercise for "High-throughput screening for potent and selective inhibitors of *Plasmodium falciparum* dihydroorotate dehydrogenase"

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1) How did the researchers use DCIP to assay PfDHODH? What other assay did they use to confirm their results?

2) In this experiment, what do the researchers define as a "hit"? What is Fig. 2, part A trying to show? (Why are all of the non-hits falling in roughly the same range of wavelengths?)

3) Use BQMOC to explain what is being shown in Fig. 2, part B.

4) Why does Fig. 4 imply competitive inhibition by the compound? Draw a picture to demonstrate how this works (as you did in the homework).

5) We have seen that the upside to targeting DHODH is that it is poorly conserved, and thus very different between humans and malaria. What might be one or more downsides of using a drug target that is poorly conserved?

6) Despite being potent inhibitors of PfDHODH, the compounds did not fare well in whole-cell assays. What did they suggest as a potential problem? Where should they go from there? If the whole-cell assay HAD worked, what would have been the next step in the drug discovery process?