In-class discussion questions for August 12, 2013
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Target-based Screening vs Whole-cell Screening

In this paper the triazolopyrimidine inhibitors were identified using target-based screening. Previously we read about the development of new methods using DAPI that allow HTS to be done using whole cells. If these inhibitors had been discovered using whole-cell screening how would that change the drug development process? Your group wants to screen a newly compiled library of compounds for malaria drug candidates using whole-cell HTS. You are competing for funding with a group that wants to screen the compound library using target-based HTS. Discuss the benefits of using whole-cell screening vs. target-based screening that you would use to argue for funding.

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Standard vs. Humanized Mouse Models

Mouse models are widely used in medical research to approximate human disease conditions. You are part of a research team looking for a new malaria drug. You want to use a standard mouse model with *P. berghei* as opposed to a humanized SCID mouse, while other members of the research team want to do the opposite.. What are the advantages of your approach? What are the downsides of the SCID mouse? Be ready to convince the other members of your team.

Standard vs. Humanized Mouse Models

Mouse models are widely used in medical research to approximate human disease conditions. You are part of a research team looking for a new malaria drug. The subject of animal testing has come up. You want to use a humanized SCID mouse instead of a standard mouse infected with *P. berghei*, while other members of the research team want to do the opposite. What are the advantages of your approach? What are the downsides of the standard mouse model? Be ready to convince the other members of your team.

Vaccine Development vs. Drug Development

You are on a committee in charge of distributing funds for a large non-profit organization with a focus on eradication of tropical diseases. There are two projects competing for funding from your organization. The first is an extension of the DHODH project. Compound 38 is a viable drug candidate in need of toxicology studies before entering phase 1 trials. The second project is a phase 2 vaccine trial using attenuated *P. falciparum* parasites given intravenously. As published in *Science* this week, "their experimental vaccine protected 12 of 15 volunteers from malaria infection, including all six receiving the most doses." You feel that the DHODH inhibitor is a better funding candidate. What are the advantages of drug development? What are the drawbacks/challenges that come with vaccines?

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