ABE591S Principles of Systems & Synthetic Biology

For class, we will be discussing 3 papers where the authors engineer the metabolism of microbes to produce value-added products. ***Students are expected to read all three papers and be prepared to discuss the major lessons in the context of the course materials***. General principles from these papers are testable! To guide the conversation, each paper is assigned to a group of students along with some questions to lead the discussion. Groups can prepare any material they would like in advance (e.g. notes, slides, etc) to lead the discussion. You may want to consult the relevant supplemental sections for each paper for detail and/or cited papers (not provided) for further details. **Each group will lead discussion for 20 minutes**. This activity is graded as part of the Journal Club Discussions.

Discussion Questions (all papers)

1. What were the main objectives of the study?
2. How do the approaches used relate to material discussed in class to date? This may include human practices/responsible synthetic biology
3. What were the main conclusions of the study? How did they achieve them?
4. Critically analyze the approaches taken. What was the motivation? What are the advantages? Limitations?
5. What are the general lessons that can be extrapolated here?

Groups

4. Dueber et al, 2009, Synthetic protein scaffolds provide modular controlover metabolic flux. ***Nat Biotech*** 27:753-759.

1. Discuss 'substrate channeling'. What potential advantages does it confer?
2. What is the metabolic bottleneck here? Why is it a critical problem? How do they overcome this?
3. What alternative strategies could the authors pursue to overcome the bottleneck?
4. What effect does scaffold architecture have on productivity?

5. Zhang, Carothers, Keasling, 2012, Design of a dynamic sensor-regulator system for production of chemicals and fuels derived from fatty acids. ***Nat Biotech*** 30: 354-358.

1. Why are the pathway intermediates toxic?
2. Describe the network motif implemented by the authors. Why is it implemented? Contrast this with advantages described for this motif in class.
3. Draw and describe the logic gate created by the authors. What are the inputs and outputs?
4. How would you apply the takeaway lessons from this paper to other systems? Is this straightforward?

6. Galanie et al, 2016, Complete biosynthesis of opioids in yeast. ***Science*** 349: 1095-1100.

1. How did they build the pathway? Discuss the metabolic engineering strategies that were used (i.e. overexpression of enzymes, feedback mutants, heterologous expression). What do these accomplish? What is the rationale?
2. How was responsible design incorporated into the project?
3. How did the authors identify the 'missing' enzyme in the pathway?
4. What challenges do the authors encounter in the heterologous expression of SalSyn?