

## Questions for discussion Lecture 1:

Discuss similarities and differences for the model of how repeat sequences affect polymorphism in genes between the two papers.

### **PNAS PAPER-DISCUSS THURSDAY AUGUST 31**

1. Why was a translational fusion between lacZ and mod constructed? Would a transcriptional fusion between mod and lacZ suffice for this study?
2. Was a transcriptional or translation fusion made with the opa gene? What would be the advantages of one versus the other for analysis of mod regulation of the opa gene.
3. In Fig. 1C “distal”, a colony shows sectoring (blue and white). Why is the colony sectored? Does sectoring frequency give you any information regarding phase variation of mod?
4. The authors performed microarray analysis to identify “target genes” regulated by mod phase variation. Does this analysis show that these genes are direct targets of regulation by mod? Can you design an experiment (either computational or experimental” to test this hypothesis?
5. The authors make a “knockout” of mod by inserting a kanamycin cassette into the mod gene. Are there advantages/disadvantages of this approach to making gene knockouts?
6. The authors state that the number of repeats affects the frequency of phase variation. Why might this be so?

### **NATURE GENETICS PAPER—DISCUSS TUESDAY SEPT 5TH**

1. Many of the cell wall protein genes identified in this study have no experimental evidence indicating they are in the cell wall of *Saccharomyces*. Using a purely computational approach, how do you think cell wall or plasma membrane proteins can be predicted?
2. Give two reasons of why the inclusion of supplemental figure 3 is important.
3. Why are multiple bands observed in some of the lanes in Fig. 2? DNA replication errors increase/decrease the number of repeats observed in these genes and therefore generate polymorphisms. Is there a process(es) that might reduce the number of polymorphisms observed in these genes over time?

4. Explain the logic and analysis in determining whether polymorphisms from “pseudogenes” could be incorporated into Flo1. Do you think pseudogenes would necessarily need to be linked to the cell wall protein gene under investigation? Why or why not?
5. Explain the URA3/5-FOA selection and why this particular system was used for the analysis of polymorphisms. Why were polymorphisms at Flo1 not assessed directly?