The polemical theorists...

- **1)** Are Hoekstra and Coyne correct in saying that there is "no compelling reason to draw a distinction between the genetic basis of anatomical versus physiological evolution?" What is Carroll's response? Is his response satisfactory? Is there a fundamental disagreement or are they just talking past each other?
- **2)** What does Carroll mean by "toolkit" genes? Are they "structural" or "regulatory"? Is it useful to classify some genes as toolkit genes?
- **3)** What array of evidence do Hoekstra and Coyne say are necessary to show that an adaptive innovation is caused by either *cis*-regulatory mutations or structural mutations?
- **4)** What is the significance of Hoekstra and Coyne's observation that most clear *cis*-regulatory mutations empirically involve a *loss* of function from the ancestral condition?
- **5)** Which of Carroll's eight principles do you find the most compelling? The least compelling?

Considering the anthocyanin pathway...

- **6)** Wessinger and Rausher's review of flower color evolution follows on nicely from Hoekstra and Coyne's note added in proof. They show that changes to white/yellow flowers are usually regulatory mutations, while transitions from blue to red flowers are functional ("structural"?) in some cases, regulatory in other cases.
 - a. Do they satisfy Hoekstra and Coyne's set of requirements in these cases?
 - b. Based on their compiled evidence, are there predictions we should make about where we will find certain kinds of mutations? That is, is it the case that some kinds of phenotypic changes are likely to be "downstream" in a regulatory pathway, and some "upstream"? Which kinds?
 - c. Do they leave us any hope that we can make predictive generalizations in phenotypic evolution?
- **7)** What implications do Wessinger and Rausher's evidence have for identifying potential evolutionary "hotspots" in genomes? (If any?)
- **8)** CREs and regulatory proteins are involved in two of the three modes of color change that W&R are examining. Would H&C call these structural or regulatory mutations? And would Carroll call them physiological or anatomical?
- **9)** What role does mosaic pleiotropy have in the mutations relevant to flower pigment change?