High resolution genetic dissection of complex and quantitative traits in yeast

Amy Sirr[1], Adrian C. Scott[1], Gareth A. Cromie[1], Trey S. Morgan[1], Russell S. Lo[1], Catherine L. Ludlow[1], Anne Clark[1,2], Joshua M. Akey[3,4], Aimée M. Dudley[1]

[1] Pacific Northwest Research Institute, Seattle, WA; [2] Department of Genome Sciences, University of Washington, Seattle, WA; [3] Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ; [4] Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ

More than 150 years after Mendel discovered the laws of heredity, the genetic architecture of phenotypic variation remains frustratingly enigmatic. Although our understanding of how genetic diversity maps onto phenotypic diversity is becoming increasingly sophisticated, substantial challenges remain. For example, while Mendelian traits can often be mapped with ease, the vast majority of biomedical, agricultural, and evolutionary phenotypes of interest are complex. The genetic dissection of complex and quantitative traits remains a formidable challenge, due in large part to the inherent complexity that governs the relationship between genotype and phenotype. Furthermore, even when successful, gene mapping studies often delimit large genomic regions, which precludes the identification of specific genes and genetic variation that causally influence traits of interest. Thus, the difficulty in moving from a quantitative trait locus (QTL) to the causal alleles influencing a phenotype presents a major barrier to a more precise mechanistic understanding of functionally and phenotypically important genetic variation. We are addressing this problem using two different approaches for genetic mapping at single gene (and in some cases sub-genic) resolution. The first is an experimental approach for refining QTL identified in forward genetic experiments by selecting only those meiotic progeny that harbor informative recombination events within a region of the genome. The use of alternative organism-specific reagents could facilitate the use of this approach in animal or plant breeding experiments. The second is the development of a large (10,000 strain) mapping population derived from a multiparent cross between eight genetically diverse yeast strains in a funnel cross design akin to the mouse collaborative cross. This resource and the statistical methods developed for its analysis will complement multiparent crosses in other model organisms, such as the mouse collaborative cross, Flyland in *Drosophilia*, and MAGIC in *Arabidopsis*.