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Editorial

Genetics Research was born as *Genetical Research* in 1960. On the occasion of its 50th birthday, we celebrate the past five decades of the journal's contributions to population, quantitative and evolutionary genetics; statistical genetics; plant and animal breeding; and genomics and general genetics – and look forward to the future. 1960 was at the beginning of the molecular revolution. While the theoretical foundations of population, quantitative and evolutionary genetics were well established, the genetic polymorphism data needed to evaluate the theories was completely missing. We now stand at the verge of another revolution, in which obtaining full genome sequences of many individuals from populations will be routine. The ten reviews in this Special Issue cover the current state of population, quantitative and statistical genetics and provide a roadmap for future research in these fields in the post-genomic era.

Model organisms offer many advantages for dissecting the genetic basis of variation in quantitative traits, including the ability to control the environment in which the individuals are raised, precisely quantify a wide range of phenotypes, and, most importantly, to measure many individuals of a defined genotype for the same trait to obtain accurate estimates of genotypic values. Bryn Gaertner and Patrick Phillips review the history of quantitative genetic analysis in *Caenorhabditis elegans*. They describe the early success in mapping and cloning quantitative trait loci of large effect for behaviors and life history traits; the biases inherent in such studies when one parent strain has active transposable elements and the other is a single realization of natural diversity; and future prospects utilizing new genetic resources and systems genetics approaches. Robert Anholt's review focuses on the genetics of olfactory behavior using *Drosophila melanogaster* as a model system to uncover general principles that underlie the architecture of complex behaviors. He reviews the results of studies using mutagenesis, gene expression analyses and association analyses of effects of molecular polymorphisms in candidate genes. These studies show that variation in behavioral phenotypes is attributable to a large number of pleiotropic loci that form epistatic genetic networks. The expression of alleles at these loci is plastic and is modulated by the sex, the social and physical environment, and the developmental history of the organism.

Gene expression levels are complex traits, with population variation attributable to both genetic variation and environmental plasticity. Gene expression provides a mechanistic link between genotype and phenotype, since variation in organismal phenotypes may be in part mediated at the level of transcription. Jinhee Kim and Greg Gibson review studies of genome wide association mapping of tens of thousands of transcripts in humans. These studies show substantial heritabilities of gene expression, with largely additive variation and an exponential distribution of effect sizes; and point to challenges to be overcome in the genetic analysis of co-regulated transcriptional networks.

Height has been used as a model complex trait in human genetics since the late 19th century, when Francis Galton used observations of resemblance among relatives to show that height has a high heritability. Peter Visscher, Brian McEvoy and Jian Yan review inferences about the genetic architecture of human height from studies of resemblance among relatives, linkage mapping, and large genome wide association studies. Genetic variation for height is primarily additive, with little evidence for dominance or epistasis; and highly polygenic, with variation attributable to hundreds of loci with small effects.

Classical quantitative genetic analyses partition phenotypic variance of trait means into genetic and environmental components. However, families, inbred lines, and quantitative trait locus alleles can also differ in the magnitude of the environmental variance for a given trait. Therefore, there is genetic variance in environmental variation, which is relevant to evolutionary theory and agricultural production. William Hill and Han Mulder review the nascent field of genetic variance of environmental variance, summarizing statistical models, appropriate experimental designs, empirical estimates, effects of selection, factors affecting the magnitude of this quantity, and issues that remain unresolved.

Molecular polymorphisms affect genetic variation for organismal phenotypes, including reproductive fitness; therefore understanding the processes that generate, maintain and eliminate these polymorphisms within and between populations are important

for understanding evolution. Brian Charlesworth reviews the history of the struggle to measure molecular variation, culminating in population based resequencing. He describes insights we have gained regarding levels and patterns of molecular variation, and the development of population genomics theory to infer the relative roles of mutation, recombination, genetic drift, and natural selection causing the observed variation.

Prior to the molecular era, progress in genetic improvement of agriculturally important animal and plant species relied on artificial selection of individuals based on their own phenotype and that of close relatives. However, we can now genotype domestic animal and plant populations for hundreds of thousands of molecular polymorphisms, and greatly improve the efficiency of artificial selection by utilizing this genetic information. With high density molecular marker information, the quantitative trait loci affecting variation in the trait will be in strong linkage disequilibrium with the molecular markers, and the markers can be used directly to predict an individual's breeding value for the trait without needing to directly map the underlying causal loci, which has proven to be exceeding difficult. This strategy is called genomic selection. Michael Goddard, Ben Hayes and Theo Meuwissen review genomic selection applied to animal breeding. They describe the statistical methodology, factors determining the accuracy of selection, implementation in breeding programs, the effect on long term genetic gain and the use of genomic selection for QTL mapping. Shizhong Xu and Zhiqiu Hu review genomic selection with a focus on plant breeding. They discuss the six major methods for genome selection (least squares, ridge regression, Bayesian shrinkage, least absolute shrinkage and selection operator (Lasso), empirical Bayes and partial least squares); describe the theory and methods for model validation; and provide an example illustrating the power of genome selection in barley.

Analyses of complex traits in model organisms often show that genetic interactions (epistasis) between mutations or quantitative trait loci are common. Further, if individuals in the same mapping population are reared in different environments, the rank order or variance of allelic effects often differs among environments (genotype by environment interaction). Modeling such interactions in mapping studies can increase the power to detect causal variants, predict phenotypic outcome, and give insight regarding underlying biology. Nengjun Yi reviews the statistical methods for high-dimensional data analysis and computational methods that can be used to model interactions, interpretation of interactions, and future research directions.

In the past decade, the amount of population genetic data on large human populations has increased astronomically, such that it is now possible to genotype individuals for 2·5 million single nucleotide polymorphisms (SNPs). While primarily used in whole genome association studies to dissect the genetic basis of complex traits, these large SNP datasets also yield insights into properties of genomes and populations, with accompanying statistical challenges. Bruce Weir and Cathy Laurie review statistical genetic analyses of these large SNP datasets, discussing issues with accounting for multiple testing and using SNP data to estimate inbreeding, relatedness and population structure.

In addition to regular research papers, *Genetics Research* encourages authors to submit topical reviews and proposals for special themed issues.

Trudy F. C. Mackay
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