nature genetics

Milestone in Anhui

Our first Nature Conference in China emphasized the value of extending genome-wide association studies (GWAS) to populations worldwide as a way to promote cooperation and high standards in research while gaining a wealth of biological insights into common and complex diseases and traits.

The meeting, held May 19–21, 2011 (http://www.natureasia.com/en/events/gwas/), began as it was originally conceived as a practical workshop with plenty of discussion time to address points our speakers raised on technical problems with existing methods for quality control, stratification control and analysis of heterogeneity (both in disease subtype and in environmental factors). It showcased the remarkable success of Chinese GWAS as the result of research investment in epidemiology and genomics and then turned to discussions of strategy, including the expected benefits of further expanding GWAS beyond populations of European ancestry, extending association methods to longitudinal cohorts and sequence-based genotyping and using mechanistic insights from GWAS to prioritize public health intervention by identifying and controlling environmental factors.

Once initial studies have met with success, it is essential to keep up the research momentum. Publications and loci identified are the beginning, not the main goal of GWAS! For example, there is plenty of biological interest (genetic architecture, environmental factors and differential survival) to be found in the data of three recent GWAS of esophageal cancer in China by Li-Dong Wang *et al.* (*Nat. Genet.* **42**, 759–763, 2010), Christian Abnet *et al.* (*Nat. Genet.* **42**, 764–767, 2010) and Dongxin Lin and colleagues (*Nat. Genet.* **43**, 679–684, 2011), and it is to be hoped that these and other groups will find common ground and common interest to maximize their analytical insights and control research costs. Participants promoted the idea of forming a GWAS consortium to promote collaboration and trust among Chinese researchers undertaking genetic epidemiology studies. It would be ideal to be able to carry out joint analyses of individual results rather than meta-analyses wherever possible as well as to encourage transparent databasing.

Many Chinese researchers said that they were worried the GWAS strategy might fall from fashion just as appropriate marker sets and study samples have been assembled to carry out their studies in China's large and diverse populations. The journal's scope and standards are constantly evolving, but we can reassure authors that the GWAS strategy is not only still productive but is itself evolving to solve ever more interesting problems. We will continue to consider each paper submitted on its individual novelty and conceptual advance as well as by the current best technical standards in the field as advised by our referees. After many years of publishing these studies, we are keen to encourage increasing collaboration between groups and to promote ever greater insights from each successive study of each trait and disease, and we are sensitive to diminishing returns as ever larger studies tackle loci with ever smaller effect sizes.

With these principles in mind, we will continue to consider for peer review genome-wide analyses of common diseases and traits not previously studied by GWAS. We are interested in studies of longitudinal cohorts and genome-wide analyses that employ a new strategy, for example, to find rarer variants using sequence-based ascertainment and novel imputation methods. We will also consider those studies with strong insights from a new population that may exhibit different linkage disequilibrium structure, genotypic architecture, allele frequencies or environmental exposures. We are interested in all strong biological insights (even from candidate studies that meet the statistical criteria for genome-wide analysis) and in the emerging field of pharmacogenetics.

Because GWAS criteria necessarily include replication, the replication of significant loci—even in a new population—is not considered by most referees sufficient to merit publication in this journal. We are less likely to send to review smaller studies finding a few significant loci after publishing a large meta-analysis. Very rare or local diseases without transferrable conceptual insight are less likely to succeed at review as are studies of non-clinical quantitative traits or traits with measurement difficulties. We are unlikely to send to review follow-up studies that complete the necessary fine-mapping and resequencing but do not add to our biological knowledge of genetic or environmental complex diseases and traits. We are unlikely to consider standard meta-analyses undertaken without participation of the data producers or new analysis methods without an application and a considerable yield of results.

In summary, the meeting was a success because it was narrow in scope but timely and had broad strategic implications. We focused on the research opportunities and practical challenges on the immediate timescale and chose GWAS, a set of techniques that have been enormously productive of biological hypotheses and international collaborations in recent years. We thank all the participants for the first of what we hope will be many successful conferences in China. ■