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► **COVER:** 'Points on view' by Patrick Morgan, inspired by the Analysis on p252.



LOUISA FLINTOFT



TANITA CASCI



MARY MUERS



MEERA SWAMI

Since the first human genome sequences were published in 2001, an overriding focus for human geneticists has been to catalogue genetic differences between individuals and relate them to differences in phenotype, particularly with respect to disease susceptibility. In this issue, a Review by Kelly Frazer and colleagues (p241) provides a big-picture view of the progress and challenges in this area.

The biggest advances have been made for common SNPs. We now have a detailed description of their genomic distribution, their frequencies and patterns of inheritance in different populations. So far, however, the same cannot be said for rare variants and structural variants. It is hoped that recent technological advances — particularly next-generation sequencing — will rapidly improve our knowledge of these variants in the next few years. The extensive cataloguing effort for SNPs has allowed genome-wide association (GWA) studies to be carried out for a range of common diseases — as a result we have gained new insights into pathological mechanisms and a good idea of how common SNPs contribute to the genetic architecture of several diseases.

In some cases, the findings of GWA studies suggest new routes to treatment or prevention. For example, the Progress article on p225 by Ming Li and Margit Burmeister describes findings that suggest potential pharmacological interventions to aid smokers in conquering their addiction. However, how the results of GWA studies should be put to clinical use is a complex issue. In their Opinion article on p264, Peter Kraft and colleagues question the practical utility of commonly used measures of the predictive value of genetic associations. They propose that alternatives to statistics such as odds ratios will generate the most informative and accurate genetic risk profiles.

#### EDITORIAL OFFICES

**LONDON** NatureReviews@nature.com  
The Macmillan Building, 4 Crinan Street,  
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