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► **COVER:** 'Along these lines' by Patrick Morgan, inspired by the Review on p370.



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Over the last few years, one term has dominated genetic thinking in the arena of complex human disease: genome-wide association (GWA). It has been said, many times, that the ability to scan the genome in an unbiased way for variants that are correlated with disease phenotypes has the potential to revolutionize our biological understanding of some of the biggest killers in the developed world, such as cancer, cardiovascular disease and diabetes.

But, in equal measure to the eager anticipation that surrounded the first crop of GWA studies, there has been a healthy amount of caution. One worry, much discussed, relates to the genetic architecture of complex disease — the GWA approach is likely to be limited to relatively common variants with modest phenotypic effects. Other concerns have focused on the way that these studies should be carried out. For example, how should cases and controls be selected? What constitutes a believable replication? And how do we move from a statistical association to a validated functional effect? Another much debated issue is how the information gathered from GWA studies can be put to use in a practical way — is the excitement about personalized genomic medicine founded, or will the small contributions of most of the variants uncovered mean that predicting susceptibility to complex disease remains a distant dream?

Drawing on experiences from the first wave of GWA papers, the Review by Mark McCarthy and colleagues on page 356 takes a critical look at these questions, highlighting areas in which consensus has been reached and those that require further attention. Much further excitement will come from the GWA approach, but careful consideration at each stage of these studies will be needed to maximize the information that will ultimately lead towards improvements in human health.

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