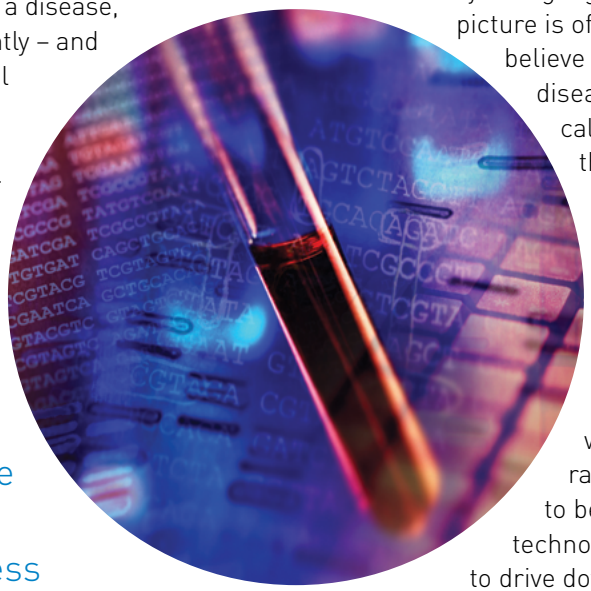
Identifying Genetic Influence on Disease

Much progress has been made in identifying the genetic causes of single gene diseases such as cystic fibrosis, phenylketonuria and Huntington disease. This has led to more accurate risk analysis, better testing approaches and, in some instances, more effective methods of treatment. Even though there are thousands of single gene disorders, they are rare, affecting less than 3% of the population.

In contrast, other diseases, including cleft lip, cardiovascular disease, psychiatric disorders and cancer, affect much of the world's population. While these diseases have a strong genetic component, they arise from a combination of genetic risk factors that are also influenced by the environment. Few of the contributing genes are believed to make more than a modest contribution to overall risk, perhaps increasing it by 5 or 10%. It is the specific combination of multiple predisposing alleles (DNA changes) and environments that leads to physical symptoms. For this reason, they are often called complex or multifactorial disorders. Identifying the factors that influence disease is a major goal for biomedical research.

Traditional methods of determining the genes responsible for single-gene disorders do not work well for complex diseases. Fortunately, thanks to the advent of second-generation technology to cheaply analyze DNA changes, scientists have used a process known as genome-wide association (GWA) to identify the genetic factors involved in complex disease.

The premise behind GWA studies: if a specific genetic variation increases the risk of developing a disease, that variation will occur more frequently – and hold up under rigid tests for statistical significance – in individuals who have the disease compared to those not affected. Basically, there is an association between the specific allele and the incidence of disease.



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Relating genetic variation to human disease and inheritance is identified in Biology COS standard 11c during investigation of disease risks from both genetic and environmental factors. This would also be appropriate discussion in AP Biology (Enduring Understandings 2e and d, 3a, b, c and 4a), Health (COS objectives 5 and 10) and the Career/Tech Intro to Biotechnology course (COS objective 14).

Touching Triton® is a serious game that has been developed by HudsonAlpha through a National Institutes of Health Science Education Partnership Award, with additional support from Lockheed Martin. This free web-based game challenges students to analyze and interpret data related to the risks for developing common complex disease. Through the storyline of long-term space flight, students learn about the complexity of risk for common disease such as diabetes, colon cancer and Parkinson disease. Students analyze data from crew members' medical record, family history and genomic report to make medical packing decisions for a 20-year space mission. More information can be found at www.triton.hudsonalpha.org.

Until recently, researchers knew of almost no genetic variants involved in complex diseases. As of 2010, over 800 genetic single nucleotide polymorphisms have been associated with more than 150 complex diseases or traits. Most of the newly associated genes had not previously been linked to the disease of interest. Intriguingly, some genetic regions have been associated with multiple disorders, suggesting common chemical pathways that influence a number of different processes.

Even with these successes, the majority of the genetic risk for common disease remains undiscovered and the contribution by a single genetic variant to the overall clinical picture is often small. As a result, scientists believe that many of the genetic risks for disease are caused by a number of so-called rare variants, genetic changes that are each present in less than 1% of the population. This view represents a shift from previous beliefs that complex diseases were caused by variants that were much more common. Projects aimed at sequencing the genomes of a larger number of individuals will hopefully identify many of these rare variants, allowing this hypothesis to be tested. In addition, as emerging technologies in DNA sequencing continue to drive down costs, many believe GWA studies will shift from examining specific sites of known genetic variation towards full sequencing of the entire genome. At that point, identifying even the rarest of variation becomes feasible.