OVERVIEW
The description of the human genome at the beginning of this millennium opened a new world of opportunity to understand the causes of common chronic diseases, including cancer, heart disease, and asthma. The early work mapped the position of human genes on the chromosomes but it did not link genes to disease. The first demonstration that this potential could be realized was accomplished at the Yale University School of Public Health when researchers identified the mutant genes that caused adult macular degeneration (AMD), the leading cause of blindness in the elderly. This seminal research was followed by the identification of other important genes, such as those linked to diabetes, Crohn’s disease, testicular cancer, and obesity. The approach to identify all of these genes followed the “genome-wide association” methodology, which had largely been pioneered by faculty at the School. In 2005 the School sponsored the first international conference devoted to this epidemiologic and statistical methodology.

Results of these studies have the potential to lead to earlier recognition, better diagnosis, and more effective therapeutic management of many chronic diseases. For example, a new biotechnology company, Optherion, has been founded in New Haven to develop therapies for AMD based on the School’s genetic research. AMD is a model for how developments in genetics can lead to rapid bio-technology transfer and impact our approaches of treating common diseases.

THE CHALLENGE
Although the foundations for the methodology of genome-wide association have been laid, the statistical work needed to pursue further genetic discoveries needs additional refinement and continued development. In addition, the gene-environment interaction has to be understood better. Chronic diseases are not caused solely by genetic variation: environmental, dietary, and other life-style factors that become harmful to health in individuals with genetic susceptibility also play a significant role. It has also become clear that single common genes are not sufficient to explain disease. The genomic model now is to look for suits of variations within many genes, each variant having only a small association with a disease, but the totality of genetic variation being needed to cause disease.

OUR RESPONSE
Finding disease genes; statistical genetics and bioinformatics
Some of the cutting-edge statistical and bioinformatics questions currently being addressed by the School’s faculty include analyses of genes in the study of disease. More complex problems in protein biology are also addressed. For example, we are developing statistical models for unraveling the genetic basis of complex
disorders, using nicotine and cocaine addiction as models for other chronic conditions. Progress is also being made on the immensely difficult task of bringing statistical order to the complex genomic and proteomic databases that derive from the micro-array technologies. Finally, several faculty members are studying tumor recurrence and have undertaken important research on how cancer and other diseases cluster in families.

**Genes and the role of the environment**

Many research groups within the School are studying the interaction between environmental agents and genes to understand certain disease pathways. Findings from these studies provide an opportunity for public health interventions to reduce disease risk. For example, the Center for Perinatal, Pediatric and Environmental Epidemiology (CPEE) is studying a range of childhood diseases: 100,000 children from pregnancy to 21 years of age from across the United States will be followed to assess the genetic and environmental causes of disease. Other diseases and conditions are studied by School faculty from the perspective of genetics and the environment. These studies include ear infections, Chlamydia, and other childhood infections, various cancers, including ovarian, pancreatic, brain, lung, bladder, and breast cancer as well as leukemia, non-Hodgkin’s and Hodgkin’s lymphoma.

**Genetics and asthma**

At CPEE three genetic regions have been identified as being associated with severe asthma. Work is continuing to genotype the whole functional genome (called whole exome sequencing) of a family of severe asthmatics and non-asthmatics using new genotyping and statistical methods, in the hope of identifying the actual single genetic variants responsible for the disease. This is a cutting-edge strategy and is only made possible because of the new genotyping methods and high speed computers available at Yale.

**WHAT WE HOPE TO ACHIEVE**

Through a better understanding of genetics and the environment, we aim to become a leader in a University-wide effort to prevent and cure diseases. Statistical and epidemiological genomics is the foundation for much of the disease research in genomics. Our goals are to support high quality research, accelerate findings that improve health, and broaden the scope of research to study more diseases with a genetic and environmental component.

**PARTNERSHIP FOR CHANGE**

Although faculty are very successful in obtaining grant support from the federal government and private foundations, substantial financial obstacles remain in the field of genomics. Among the urgent priorities for endowment support are:

- Scholarship support for pre- and post-doctoral students who can be trained in genetic epidemiology to become the next generation of faculty in our universities
- Support for new faculty who are beginning their careers and who need start-up funds for the pilot projects that will lead to larger grant applications
- Infrastructure support for the high technology equipment needed for genetic and proteomic studies, including state-of-the-art computational equipment
- Major support for professorial chairs in these areas of research so that the School and Yale can attract and retain the world’s brightest scholars in a highly competitive environment.

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