2012- Human Genetic Variation and the Inherited Basis of Disease
David M. Altshuler, M.D., Ph.D.

David Altshuler, a clinical endocrinologist and human geneticist, is a founding core member of the Broad Institute and has directed the Broad’s Program in Medical and Population Genetics since 2003. In 2009 he was named the Broad’s first chief academic officer.

Altshuler studies human genetic variation and its application to disease, using tools and information from the Human Genome Project. He has been a leader in The SNP Consortium, International HapMap Project, and 1000 Genomes Project, public-private partnerships that have created public maps of human genome sequence variation as a foundation for disease research. On this foundation, he and his colleagues have developed laboratory tools and analytical methods necessary to enable the systematic study of human genetic variation for its role in common diseases. He has discovered gene variants that influence the risk of common conditions, including type 2 diabetes, blood cholesterol, heart attack, prostate cancer, systemic lupus erythematosis, and rheumatoid arthritis.

Altshuler has been on the faculty of Harvard since 2000 and is currently a professor of genetics and medicine at Harvard Medical School, and in the Department of Molecular Biology, the Diabetes Unit of the Department of Medicine, and the Center for Human Genetic Research, all at Massachusetts General Hospital.

Among his honors are election to the American Society for Clinical Investigation, the Association of American Physicians, and the US Institute of Medicine. He is a member of the Board of Directors of the American Society of Human Genetics and Vertex Pharmaceuticals. He has served in many advisory capacities, including on the Advisory Council of the NIDDK (National Institutes of Health), the Strategy Committee at the Wellcome Trust, and the Board of Reviewing Editors at Science. He was awarded the Curt Stern Award from the American Society of Human Genetics and the Outstanding Scientific Achievement Award from the American Diabetes Association.

Altshuler received his B.S. from MIT, Ph.D. from Harvard University, and M.D. from Harvard Medical School. He completed his internship, residency, and clinical fellowship training at Massachusetts General Hospital.

Abstract

Despite great progress in medical science, we have limited knowledge of the molecular causes of most disease in human populations. This ignorance is one of the gating factors in efforts to design rationale approaches to prevent and treat disease. Genetic mapping offers an approach to study disease that is (a) unbiased by prior hypotheses about disease mechanisms, and (b) supports causal inference directly in the human population. We have worked to make possible genetic mapping of common diseases by developing maps of human sequence variation (the SNP Consortium HapMap, and 1000 Genomes Projects), and by developing technologies and analytical methods to enable genome-wide studies that relate genetic variation to diseases. Over the last five years the first generation of these methods (based on common SNPs, and on copy number variations) have led to the identification of over 1,000 novel and reproducible associations between genomic regions and a wide variety of common diseases, including our own work on type 2 diabetes, hyperlipidemia, prostate cancer, age related macular degeneration, rheumatoid arthritis, and systemic lupus erythematosis. We are now focusing on discovering the genes and mutations responsible at each locus, extending the mapping approach to query rare genetic variation using next-generation sequencing, and to studies spanning multiple ethnic groups. More fundamentally, with the widespread success of genetic mapping for common diseases, the rate-limiting step has already shifted from the discovery of novel genes to the application of this information to gain new insights into disease mechanisms, with the ultimate goal of developing new and more effective approaches to prevention and treatment of disease in the population.