2011 Introduction to Curt Stern Award[1]

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Good afternoon and welcome. I am Aravinda Chakravarti, and on behalf of the American Society of Human Genetics, I have the great pleasure of introducing to you a friend and collaborator, Dr. David Matthew Altshuler, recipient of the 2011 Curt Stern Award. This award is given annually by the ASHG in recognition of major scientific achievement in human genetics in the last ten years. In honoring David, we recognize his contributions to three major areas: (1) making systematic studies of common human genetic variation possible, (2) defining the genetic contributions to type 2 diabetes and other common disorders, and (3) enabling a model of collaborative team science in human genetics. David Altshuler is currently a professor of genetics and medicine at Harvard Medical School and deputy director and chief academic officer at the Broad Institute.

First, a bit about Curt Stern (1902–1981): Stern was a well-known and highly accomplished fly geneticist before he turned his attention to human genetics. He demonstrated physical crossover of homologous chromosomes in *Drosophila melanogaster* only weeks after McClintock and Creighton had done so in maize, demonstrated mitotic recombination resulting in somatic mosaics, and demonstrated the mechanism of dosage compensation. During World War II, he led research on low-dose-radiation safety to conclude that there was no "safe" threshold. He was a pioneer of gene-regulation studies, which focused his interests on human genetics, and a pioneer in teaching genetics to medical students, resulting in the book "Principles of Human Genetics." Curt Stern served as the 1957 ASHG president.

And now to David Altshuler: I first met David at 9:45 am on Thursday, May 6, 1999 in Cambridge, MA. At the time, he was a second-year postdoctoral fellow with Eric Lander at the Whitehead Institute. He was learning human genetics and the mapping of hereditary disorders by using genomic tools. David arrived at the Whitehead after completing his M.D. at Harvard University in 1994, his Ph.D. with Connie Cepko on vertebrate rod photoreceptor development in 1994, and his internship, residency, and clinical fellowship in endocrinology at Massachusetts General Hospital in 1999. I remember from our first discussion that David's interests in the genetics of common disease were quite clear.

The scientific question in 1999—yes, 12 years ago—was whether human disease mutations were more like those in *BRCA1* (rare) or *APOE* (common). When speaking to a reporter (Steve Olson, who was writing for the 2000 Summer Bulletin of the Howard Hughes Medical Institute), David said, "Whether such mutations could have been found by a dense SNP map is an area of intense interest. What we need are more data so we can understand the issues better and then determine how to proceed."

The task of obtaining these data was much more complicated than anyone chooses to remember. The genome sequence was not in hand, and there were numerous biotech companies vying to generate and make their own genomic and SNP databases private.

It is in this background that David Altshuler began his own studies and provided leadership for the SNP Consortium that began in 1999 as a collaboration between several companies and institutions to produce a public resource of SNPs in the human genome. The rest is history. This led to the intimate involvement of the NIH and the Wellcome Trust in the International HapMap Project and later in the 1,000 Genomes Project. David's efforts in creating a resource of common and rare genetic variants in humans and the associated human-population genetics that allowed interpretation of these data are of universal value to our science.

The availability of dense catalogs of human genetic variants has spurred numerous studies in his laboratory and in others. The most notable studies have been those on patterns of linkage disequilibrium within and between human populations, on the distribution of recombination across the human genome, on the detection of natural selection, on the estimation of group admixture, and on numerous reconstructions of human history. However, the studies most important to David have been those that have allowed genetic dissection of numerous common diseases, including his own passion, type 2 diabetes. These studies have also brought new controversy to our field. Why don't these studies explain all of a disease? Why do the genetic variants have such

[1]This article is based on the address given by the author at the meeting of the International Congress of Human Genetics on October 13, 2011 in Montreal, Quebec, Canada. The audio of the original address can be found at the web site of the American Society of Human Genetics.

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small effects? I have faith and patience that we will answer these questions, as will David, and the answers will come from using current clues to understand disease mechanisms and not from merely counting. Already, many genome-wide association studies have been very illuminating in uncovering human biology that we neither guessed nor could imagine. Finally, the new common-disease studies have demanded a cultural change in our practice of science and have required a level of cooperation and collaboration unknown and unfamiliar to our field. In all of this, David Altshuler has played a leading and remarkable role.

Ladies and gentlemen, please join the ASHG and me in congratulating David Altshuler for significant contributions to our field of human genetics and as the 2011 Curt Stern awardee.