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David Botstein blurts out his thoughts unfiltered. Sometimes they change the world.

In 1978, David attended a retreat of the University of Utah's Biology Department, where he heard a speaker bemoan the difficulty of determining whether the human disorder hemochromatosis was inherited in a recessive or dominant manner. David blurted out: "Of course, it would be simple to tell if you had a linked genetic marker!" A beat later, a light bulb went off in his head. The previous year, David had done an experiment in yeast in which he had used a polymorphic DNA site as a marker to map the location of a centromere. In principle, he realized, the same approach might work in humans.

Two years later, in 1980, David published a landmark paper proposing the construction of a comprehensive genetic linkage map of the entire human genome based on mapping DNA polymorphisms in human families—a general tool that could be used to find the location of the gene responsible for any simple Mendelian disease.

It was also the origin of the Human Genome Project—the first time that someone proposed creating a genome-wide map of the human chromosomes. The idea soon led to the mapping of the gene for Huntington's disease to the tip of the short arm of chromosome 4 in 1983, the gene for cystic fibrosis to chromosome 7 in 1985, and ultimately to the mapping and later molecular cloning of the genes underlying more than 3000 Mendelian diseases. And, it sparked the HGP, because it made us realize that knowledge of the human genome would have a transformative impact on medicine and that the genome itself is finite and determining its sequence a tractable task.

David's unique gift for thinking out loud exasperates some people, because he can express half-baked ideas with the certainty of eternal verities. But, Botstein connoisseurs relish the chance to directly observe the cortical neurons firing in the brain of one of the world's best geneticists. And his extraordinary insights are matched by his utter integrity, as a scientist and as a person.

Apart from finding my wife, the luckiest thing that ever happened to me was being introduced to David Botstein after a weekly biology colloquium at MIT in 1985. After being told that I had been trained as a mathematician, David made some pronouncement about the issues in mapping polygenic traits. We immediately fell to arguing. We had so much fun we got together to argue more the next day. I soon dropped everything else I was working on to pursue human genetics—and went on, within a few years, to launch what would become one of the world's leading genome centers. I shudder to think what would have happened to me if I had not met David Botstein.

In this, I know that I am not alone. David has touched so many scientific lives and shaped our entire field.

By Eric Lander