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A Haplotype Map of the Human Genome – Biomedical Tool for Genetic Research in Canada

Status	Past
Competition	Competition II
Sector	Health
Genome Centre	Genome Quebec
Project Leaders	Thomas Hudson

Project Description

The DNA inside our trillion cells contains long chains of four chemical building blocks, known by the letters *A*, *T*, *C* and *G*. More than 6 billion of these chemical bases are strung together like pearls on a string inside the nucleus of each cell.

The challenge for scientists has been to find patterns in the apparently random order of the bases. Although the genetic sequences of different people are remarkably similar, it is the differences — the variations — that continue to interest researchers.

That's because our DNA contains information that influences everything from our physical appearance to the likelihood of our contracting a particular disease. When one letter is out of sequence — for example, a *G* occurs where other individuals have a *T* — scientists call this variation a “Single Nucleotide Polymorphism,” or “SNP” for short.

There are so many of these tiny one-letter variations – an estimated 10 million – that testing to look for differences is simply too expensive and inefficient. And early on, scientists learned that these variations are not scattered uniformly throughout our genes. Instead they tend to be clustered into blocks of DNA called Haplotypes.

What researchers needed was a kind of map – a catalog of common Haplotypes to make large-scale genomic association studies possible.

Launched in 2002, the international HapMap Project began by collecting data from four populations in different parts of the world. The three-year study cost \$138 million and involved a consortium of scientists from Canada, China, Japan, the United Kingdom, the United States and Nigeria. In October 2005, the first comprehensive catalogue of genetic variations was published in the prestigious journal *Nature*.

Traditionally, geneticists have tracked the inheritance of a genetic disease through large families or searched for suspected problematic genes among patients. Genome-wide association studies go much further. They compare the distribution of SNPs (pronounced “snips”) in

hundreds or even thousands of people with and without a particular disease. By tallying which SNPs occur with symptoms, researchers can determine how much increased risk is associated with each SNP.

In October 2007, the results of phase II of the HapMap were published in Nature. Because it contains three times more genetic markers than the first version, the higher resolution of this second version offers a greater ability to detect the minute fraction of human genetic material that varies among individuals, variations that could explain the differences observed in disease susceptibility and drug response. It also makes it possible to learn how certain environmental factors influence the human genome.

Heading the Canadian contribution to the project was Dr. Tom Hudson, Director of the McGill University and Génome Québec Innovation Centre. He calls the HapMap “a major breakthrough for scientists. It’s as significant as sequencing the human genome.”

That’s because the HapMap not only identifies variations, but where they occur in our DNA, allowing scientists to determine which of them may be related to a particular disease. “This is really a map to study the genetics of common diseases,” Hudson explains.

For instance, by comparing the Haplotypes in individuals with high blood pressure to the Haplotypes of a comparable group of healthy people, scientists are beginning to pinpoint which genes are associated with the disease. Identifying specific disease-causing genes, in turn, will lead to better ways of predicting, diagnosing and treating illnesses.

The HapMap Project has already yielded several groundbreaking discoveries. Dr. Hudson and his collaborators have identified genes involved in Type 2 diabetes and colon cancer. Other scientists around the world have relied on HapMap to identify common genetic variations for diseases including macular degeneration, the leading cause of blindness in seniors, tuberculosis, coronary heart disease, Type 1 diabetes, rheumatoid arthritis, Crohn’s disease and ulcerative colitis, and bipolar disorder.

Exploring the vast landscape of our genes is difficult work. But like any traveller, scientists have discovered it’s much easier when you know where to look for directions. And that begins with a good map.

Fast Facts

Highlighted outcome: a powerful tool to help researchers around the world find genetic causes for complex diseases

Number of research personnel employed by the project: 26

Number of peer reviewed publications published: 21 peer-reviewed manuscripts, 34 abstracts, 53 invited presentations

Number of patents in process or obtained: 1 patent disclosure for Nanuq, a platform for genotype query, storage and analysis