The Problem
Differences in our genome sequences, or genetic variants, have a profound influence on many human traits such as height, blood pressure and disease risk. Yet there are millions of genetic differences between individuals and it is difficult to determine which of them are important. Recently, geneticists have made tremendous progress in this area by sequencing the genomes of thousands of individuals. Many genetic variants are now associated with human traits, however, in most cases we still do not understand how these variants function. Unraveling how genetic variants affect molecular processes within human cells will give us a new understanding of health and disease.

The Approach
Graham McVicker is developing innovative computational and statistical techniques to unscramble the molecular function of human genetic variation. McVicker is specifically interested in understanding how genetic variants affect chromatin in the immune system. Chromatin is the molecular packaging that organizes DNA within the nucleus of the cell and controls which genes are turned on in specific cells. By gaining a mechanistic understanding of these variants and linking them to disease risk, he will illuminate why some individuals are more susceptible to autoimmune and infectious diseases.

The Innovations and Discoveries
- McVicker previously discovered human genetic variants that affect chemical modifications of an important type of protein of chromatin, called histones. He showed that many of these variants disrupt the binding of specific proteins to the DNA sequence and also affect the expression of nearby genes.
- He identified factors that are important for positioning nucleosomes—the fundamental units of chromatin—on the human genome sequence.
- He demonstrated that natural selection has influenced patterns of genetic variation across the human genome.

For more information, please visit:
http://www.salk.edu/faculty/mcvicker.html