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Towards Single Cell Genomics

Status	Current
Competition	Development of New Technologies Competition
Sector	Development of New Technologies
Genome Centre	Genome British Columbia
Project Leader	Carl Hansen & Marco Marra

Project Description

Cells are the building blocks of life. Within all creatures and plants, collectively called "organisms", there are large numbers of cells that work together to allow the organism to develop and function. In humans, it is thought that there may be as many as 100 trillion (100,000,000,000,000) cells. This implies that cells must be small. In fact, about 60,000 human cells can fit on the head of a pin. To perform the complex functions of the organism, some cells must take on specialized roles. In mammals, for example, liver cells perform different roles than brain cells, and heart cells perform different roles than skin cells. But, even within tissues, there are specialized cells. For example, in human blood, there are red cells, T cells, B cells, plasma cells, and so on. All of these cells have important roles in normal development and health. The overall control of how cells become specialized as organisms develop is not well understood, but this control must in general function reliably to avoid disease and ensure the ability to reproduce.

In general, all of the cells within sexually reproducing organisms receive one complete set of genetic instructions from each parent. This complete set of genetic instructions is called the genome, and the scientific approach to studying the genome is called genomics. The genome is composed of DNA and contains the code for genes.

It is known that cells within an organism become specialized, and hence different from each other, as a consequence of turning certain genes on or off. Genes that are turned on are said to be "expressed", and this expression can be measured by looking for the presence of another molecule called RNA, which is produced from a gene when it is turned on. Disease can result if the wrong genes are expressed or have their expression turned off. Many scientists have used the tools of genomics to discover which genes are expressed within normal and diseased tissues as a way to identify the genes that are mistakenly turned on or off in diseased tissues. Some of these studies have eventually resulted in drugs which are designed to interfere with genes when they are mistakenly turned on. Gleevec, which is used to treat leukemia, is an example of such a drug.

One critical problem that scientists face in identifying the genes whose mis-expression results in disease is the very small size of individual cells. This small size means that very little RNA is present, much less than can be studied using the current tools of genomics. Another critical problem is that within a tissue there are typically many different types of cells, only one of which may be relevant to the disease process. For example, many cancer tissues contain confusing mixtures of normal and diseased cells, and scientists studying gene expression in such cancers are most likely mis-led by this confusing mixture. In fact, discovery of the most important mis-expressed genes in such tissues is usually impossible.

Our project, which involves leading experts in genomics and engineering, proposes to solve these critical problems by developing a new approach that will allow scientists to apply the tools of genomics to many single cells at once. By studying single cells we hope to avoid the confusion that accompanies the study of complex mixtures of cells, and more accurately measure the RNA that is present within each cell. Broad availability and application of our approach will allow scientists to accurately measure RNA in single cells, which will in turn lead to a dramatically improved ability to identify mis-expressed genes in diseased tissues. This will eventually produce high quality gene targets for the design of new drugs. We foresee that our approach has the potential to revolutionize many areas of research in addition to health care, including examination of genomic differences in "normal" non-diseased tissues, and in studying the genomes of un-culturable microbes inhabiting interesting ecological and environmental niches.