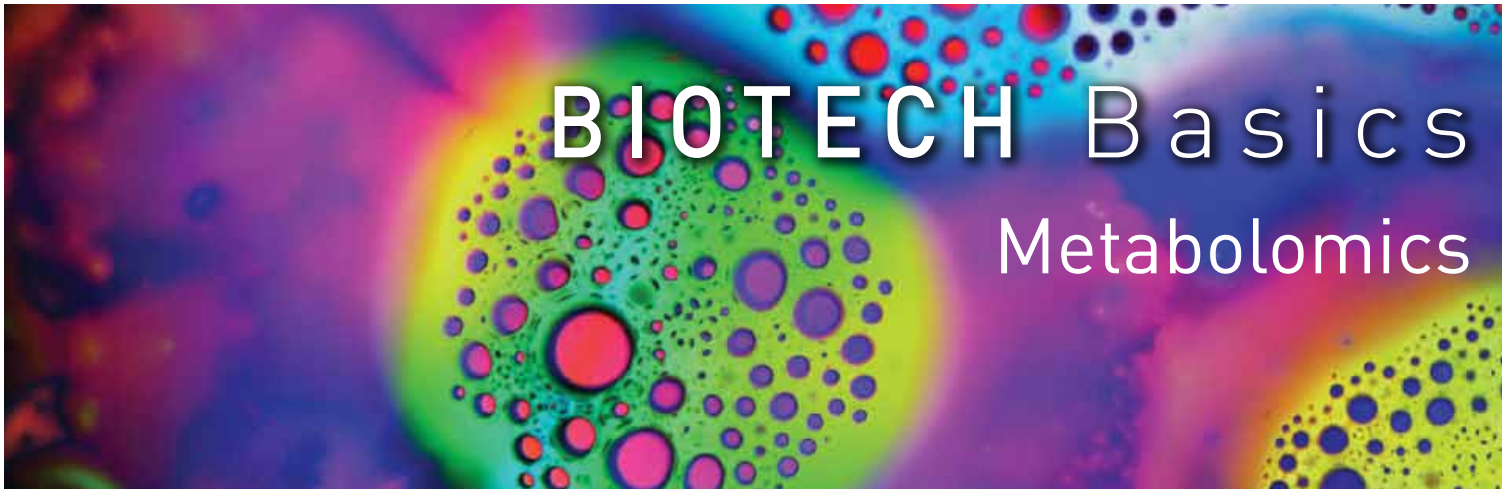

BIOTECH Basics

Metabolomics

What You Need to Know

- *As cells grow and divide, they produce small chemical molecules known as metabolites.*
- *The number and amount of these metabolites change under varying conditions such as diet and environment, and in response to disease.*
- *The relatively new field of metabolomics seeks to identify and catalog these metabolites, with a goal of linking specific molecules to health and disease.*
- *Metabolomic studies will soon begin at HudsonAlpha, with the addition of Dr. Sara Cooper as a new faculty investigator.*

For more information:

www.metabolomics.ca
www.hmdb.ca

The Human Metabolomics Project provides an overview of how metabolomics relates to human heath and disease. The Human Metabolome Database is an electronic database containing information about the various metabolites identified in the human body. Both are supported by Genome Canada, a non-for-profit organization that oversees Canada's genomics approach.

Most of our *Biotech Basics* articles have focused on genetics and genomics, or the study of DNA and RNA in our cells. This time we will look at a different class of molecules called metabolites. As our cells live, grow, and divide – the process of metabolism – they release a number of small molecules including lipids (pieces of fats), amino acids (pieces of proteins), and other chemicals produced during the reactions that provide energy for the cell. Just as technology emerging in the last 15 years allows us to simultaneously study the genome, or all the genes of a person, we can now study the metabolome – all of the metabolites (see next page for other important "-omes").

As of October 2010, the Human Metabolome Database (hmdb.ca) listed over 7900 chemicals as small molecule metabolites found in the human body.

A window into cell activities

Metabolomic studies can give us a snapshot of what's going on in cells, tissues, organs or an entire organism. The relationship between changes in our DNA and changes in our metabolites is not a straightforward one. While a single base change in DNA may only alter one amino acid in a protein, it may result in a huge change in the activity of that protein and the resulting interactions with other cellular components. Consider sickle cell anemia: One DNA change in the beta-globin gene changes one amino acid in the hemoglobin protein, which carries oxygen in our blood cells. In patients with two such altered hemoglobin genes, the red blood cells at times are shaped like crescents or sickles rather than the usual doughnut shape, hindering the cell's ability to carry oxygen through the bloodstream. Recent metabolomic studies have shown that this one protein change goes even further and impacts multiple pathways important to the cell. These data can be useful in managing the care of sickle cell patients. For years, doctors have seen patients develop symptoms that appear unrelated to oxygen utilization. Metabolomic research may provide clues to why these symptoms appear and how to treat them.

How the metabolome is studied

In order to study metabolites, researchers often use a technique called mass spectrometry, which separates most of the molecules in a sample by their varying size (mass) and electrical charge. Let's say we wanted to compare urine samples from two groups of people, to see if we can detect markers that are different between their respective metabolisms. After some basic laboratory preparation, a portion of each sample would be loaded into

the mass spectrometer, a machine about the size of a dorm refrigerator. The sample is literally vaporized, and shot down a tube past a beam of positively charged ions. Collectors at the end of the tube measure how fast the molecule traveled – based on its mass – and how much the molecule was deflected away from the positive charge, based on its own charge. By adding those two variables, we can figure out the probable identity of each molecule. The results are plotted as a series of peaks on a graph, with each peak corresponding to a different molecule (see figure).

Metabolomic clues for prostate cancer

A recent example of this type of experiment was published in the journal *Nature* in February 2009. Researchers looked at both urine and tumor samples from patients with prostate cancer, specifically to see if any metabolites could predict progression of the disease. One can imagine that as cancer cells grow and spread, their metabolism is altered, producing different levels of metabolites that could be detected and used as a marker for the disease. Using mass spectrometry and similar techniques (plus lots of computational analysis!), the researchers pinpointed a chemical called sarcosine as being correlated with stage of prostate cancer. They and other groups are now investigating if sarcosine is truly important in prostate cancer progression, or is just a byproduct of another process. Either way, they will also determine whether an accurate and useful clinical test based on levels of sarcosine can be developed.

Metabolomics and HudsonAlpha

HudsonAlpha has recently recruited Dr. Sara Cooper to study metabolomics in both yeast and humans. While many of our studies at HudsonAlpha look at DNA or RNA from the cell as a marker for disease, we are excited to add the capability to look at metabolites from cells as well. As noted above, the relationship between the genome and the metabolome is not always a direct one, and being able to look at cells from multiple approaches aids the ability to identify causation and treatment for disease. Cooper has previously examined how deleting each gene of the yeast genome, one by one, impacts the cell's metabolism. Her findings were published in the journal *Genome Research* in September 2010. She plans to build on this work, and explore extensions to human disease, using HudsonAlpha's latest piece of technology – our very own mass spectrometer.

Important "–omes" for Biology

Genome - all of the chromosomal DNA in the nucleus

Transcriptome - all of the RNA produced from the DNA in a cell.

Proteome - all of the proteins in a cell.

Metabolome - all of the metabolites, or small molecules, produced by a cell in process of metabolism.

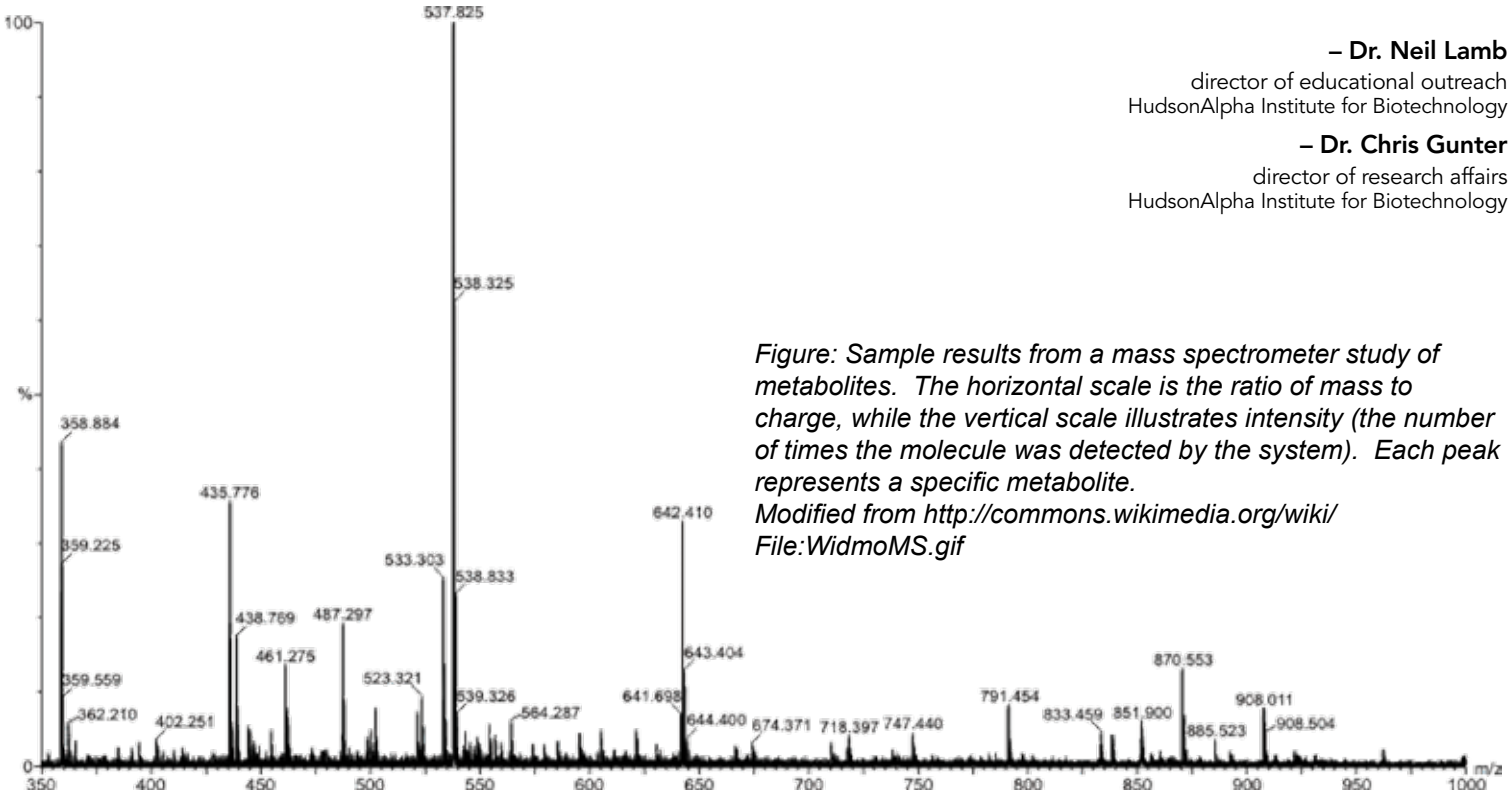

Figure: Sample results from a mass spectrometer study of metabolites. The horizontal scale is the ratio of mass to charge, while the vertical scale illustrates intensity (the number of times the molecule was detected by the system). Each peak represents a specific metabolite.
Modified from http://commons.wikimedia.org/wiki/File:WidmoMS.gif

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