

Science Education Collection

An Introduction to Cell Metabolism

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Abstract

In cells, critical molecules are either built by joining together individual units like amino acids or nucleotides, or broken down into smaller components. Respectively, the reactions responsible for this are referred to as anabolic and catabolic. These reactions require or produce energy typically in the form of a “high-energy” molecule called ATP. Together, these processes make up “Cell Metabolism,” and are hallmarks of healthy, living cells.

JoVE’s introduction to cell metabolism briefly reviews the rich history of this field, ranging from early studies on photosynthesis to more recent discoveries pertaining to energy production in all cells. This is followed by a discussion of some key questions asked by scientists studying metabolism, and common methods that they apply to answer these questions. Finally, we’ll explore how current researchers are studying alterations in metabolism that accompany metabolic disorders, or that occur following exposure to environmental stressors.

Transcript

Cell metabolism refers to the vital metabolic reactions that occur within a cell. When most people think of “metabolism,” they associate it with the “burning” or breaking down of nutrients. However, in cell biology metabolism encompasses “catabolism,” which is the breaking down of molecules, and “anabolism,” which is the synthesis of new biological compounds. These processes provide cells with energy, and help build their components, respectively.

This video will delve into the major discoveries that have contributed to our understanding of cell metabolism. We’ll follow this up with an examination of key questions in the field, and some of the techniques currently used to study metabolic pathways.

Let’s dive into the rich history of cellular metabolism.

Between 1770 and 1805, four chemists performed key experiments, which helped to explain how plants produce “mass” to grow. Their work led to the basic photosynthesis reaction, which established that in sunlight, plants take in carbon dioxide and water, and produce oxygen and organic material. Later in the 1860’s, Julius von Sachs determined that this organic material was starch, which is composed of the sugar glucose.

So, plants produce sugar. But, we consume it. So what happens to the sugar in our bodies? A potential answer came in the 1930’s, when Gustav Embden, Otto Meyerhof, and Jacob Parnas described glycolysis, the pathway that breaks down glucose into pyruvate. We now know that glycolysis also produces adenosine triphosphate or ATP.

ATP’s structure was determined in 1935 in Meyerhof’s laboratory by Karl Lohmann. Meyerhof and Lohmann proposed that ATP could “store” energy, which was confirmed by Fritz Lipmann in 1941, who identified the energy-rich bonds in ATP and provided a theory by which these bonds could be harnessed during biosynthesis.

In parallel, Hans Krebs found that the oxidation of glucose or pyruvate could be stimulated by a number of acids, all of which are a part of cyclic reactions forming the tricarboxylic acid cycle, abbreviated as the TCA cycle. His major contribution was noting that oxaloacetate and pyruvate could be converted to citrate, which gave this oxidation series its cyclical form.

In 1946, Lipmann and Nathan Kaplan further elucidated the reaction converting pyruvate to citrate with their discovery of coenzyme A. We now know that pyruvate interacts with this enzyme to form acetyl-coenzyme A, which launches the TCA cycle.

Later, between the 1950’s and 1970’s, researchers determined that electrons released during the TCA cycle could be “carried” to protein complexes located in mitochondria in a pathway called the electron transport chain. Importantly, in 1961 Peter Mitchell proposed that the transfer of electrons between these complexes produces a proton “gradient,” which could drive the production of the majority of a cell’s ATP.

Taken together, the discoveries of photosynthesis, glycolysis, the TCA cycle, and the electron transport chain have formed the foundation upon which today’s studies of cellular metabolism now rest.

Although these historical discoveries have provided immense insight into metabolic pathways, they have also spurred several questions. Let’s review some of those that remain unanswered.

Today, researchers are looking at how metabolic pathways are affected by environmental stressors like toxins or radiation. In particular, there is interest in how such factors result in the abnormal production of reactive oxygen species like free radicals, which possess unpaired electrons on oxygen atoms, making them highly reactive. These molecules can damage other cellular components and result in oxidative stress.

Oxidative stress has been implicated in cellular senescence and death, and also in the initiation and progression of cancer. Therefore, cell biologists are interested in determining how these reactive species affect a cell’s normal physiological processes, such as cell division. With this information, they can further deduce the role of these species in pathological events.

Finally, several researchers are interested in metabolic disorders—conditions in which specific metabolic reactions are disrupted. These include diseases like diabetes, where the body is unable to metabolize sugar. Researchers are currently trying to identify factors, such as genes or environmental cues, which contribute to such diseases. This will ultimately help them in developing more effective therapies for patients.

Now that you've heard a few pressing questions in the field of cellular metabolism, let's review the experimental techniques scientists are using to address them.

The ultimate goal of many catabolic processes in live cells is to generate ATP, which is the primary energy storage molecule used by cells. Therefore, techniques like the ATP bioluminescence assay, which quantifies ATP in a sample with the help of a luminescence reaction, can provide insight into cells' metabolic activity.

Other methods focus on specific metabolic pathways. For example, researchers can evaluate the metabolism of glycogen into its monomer glucose. One way to do this is to process glucose derived from glycogen into products that will react with detecting probes and induce a color change or fluorescence. In this way, researchers can calculate how much glycogen was originally present in their samples.

In contrast, abnormal metabolism can be detected by measuring reactive oxygen species. Commonly, researchers use a probe that fluoresces after being "attacked" by a member of these species. These assays directly quantify the amount of reactive oxygen metabolites, and therefore help in the detection of oxidative stress.

Finally, researchers analyze metabolism at the organismal level by "Metabolic Profiling." With the help of advanced methods like high performance liquid chromatography or HPLC, and mass spectrometry or MS, scientists can quantify metabolites present in biological samples, and determine if certain metabolic pathways are stalled or overactive.

With all of these tools at their disposal, let's see how scientists are putting them to experimental use.

Some scientists are applying these methods to develop new ways to diagnose metabolic disorders. Here, a protocol was developed to isolate peripheral blood mononuclear cells, or PBMCs, from patient blood samples in order to assess their glycogen content. By using a glycogen metabolism-specific staining assay, researchers gained insight into the amount of glycogen present in these samples. In future applications, this technique could help diagnose patients with glycogen metabolic diseases.

Other researchers are using these tools to study the effect of environmental stress on metabolism. In this experiment, scientists measured reactive oxygen species in zebrafish embryos treated with a chemical called rotenone, or following damage to their tails. This was done with the help of a probe that fluoresces red when targeted by reactive oxygen species. Subsequent assessment of whole embryos revealed increased production of these molecules in response to injury and chemical exposure, suggesting a protective role of these metabolites.

Finally, cell biologists are also studying the metabolic characteristics of cancer cells. Here, researchers collected the contents of human colon cancer cells, and subjected this extract to metabolic profiling using HPLC and MS. This allowed researchers to identify metabolites present in this diseased tissue.

You've just watched JoVE's introductory video to cellular metabolism. Many complex pathways describe the metabolic activity of cells, and now you know how these pathways were discovered, and how researches are still trying to decipher the unknown components. Remember, metabolism is good, but excess of anything can be harmful. As always, thanks for watching!