

March 27, 2008

## Teasing out the structure of a crucial protein

*Researchers at RIKEN's SPring-8 Center clarify a process in cells important in drug discovery research*

Scientists in Japan have made progress in understanding a complicated biochemical process important in the metabolism of cells. The process, known as biotinylation, is important in the functioning of a class of enzymes that participate in the transfer of carbon dioxide between metabolites in cells. Metabolites are substances essential for the functioning of a cell's metabolism, and are also products of cell metabolism.

The scientists, from RIKEN SPring-8 Center in Hyogo Prefecture, Japan, analysed protein structures using radiation from the SPring-8 synchrotron facility.

A better understanding of the biotinylation process is important for the development of new types of drugs, particularly those related to obesity and diabetes. The enzymes involved are known as carboxylases because of their role in the CO<sub>2</sub> transfer process. Carboxylases in humans are one focus of research into these types of drugs. It is important for scientists to have a better knowledge of the three-dimensional structure of these enzymes for this purpose, and it is here that the RIKEN team has made a significant advance.

Biotinylation refers to the process of adding biotin to a surface or molecule. Biotin is a crystalline vitamin related to vitamin B, and is found in liver, egg yolk, milk and yeast. It is important in the functioning of many enzymes in the cell's metabolism. Biotin is also important in many aspects of human health, including promoting healthy cell growth and bone marrow growth. It is also used as a treatment for some skin conditions such as eczema and dermatitis. Biotin deficiency can lead to extreme tiredness and muscle pain, as well as loss of appetite. The RIKEN team focused on a substance named biotin protein ligase, which is very specific in its action. It acts as a catalyst for the biotinylation process, at only a very specific site on the target molecule.

The team was able to establish three-dimensional structures for a number of the complex substances involved in protein biotinylation. They also were able to make progress in determining the complex processes involved. However, the exact sequence

of events involved in the process remains a challenge for future research.

As researchers continue to shed light on these molecular-level processes within the cell, the implications for medical science are likely to be considerable, particularly regarding protein engineering. In addition to the development of designer drugs, there are applications in purification of proteins. There are also implications for a method known as molecular imaging using quantum dots, which has already proved a powerful method for tracking disease-related molecules inside cells. As these techniques are further refined, medicine will inevitably be transformed.

**Original work:**

Bagautdinov, B., Matsuura, Y., Bagautdinova, S., Kunishima, N. Protein Biotinylation Visualized by a Complex Structure of Biotin Protein Ligase with a Substrate, *The Journal of Biological Chemistry*, published online on Mar. 26, 2008

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