Synthesis of Selenocysteine-containing Proteins and their Properties

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Biography

Hironobu Hojo obtained his PhD in organic chemistry from Osaka University, Japan in 1994, under the guidance of Prof. Saburo Aimoto on the development of the chemical method for protein synthesis. After the completion of his PhD, he moved to the Osaka City University as lecturer and worked on the development of novel biomaterials. In 1998, he moved to Tokai University, Japan, as an associate professor. There, he started to develop a facile method for glycoprotein synthesis by collaboration with Prof. Yoshiaki Nakahara. He was promoted to professor of Tokai University in 2007. He moved to the present position, Professor of the Institute for Protein Research, Osaka University, in 2013 and is developing a chemical approach toward the understanding of protein and glycoprotein function.

Abstract

The substitution of disulfide bond to diselenide bond in peptide and protein is quite isomorphous in point of their structure and biological activity, which was demonstrated in the case of several peptides, such as endothelin [1] and conotoxin [2] by several researchers. One of the advantages of diselenide substitution is that it is more resistant to reduction. The above researches also showed that the diselenide cognates retained higher stability under reducing conditions as well as in blood plasma. In this presentation, I will talk about the synthesis of several diselenide cognates of natural proteins.

One is a selenoinsulin, in which one of the interchain disulfide bonds of the native insulin were substituted by diselenide bond [3-4]. We first synthesized A and B chain separately incorporating one selenocysteine (Sec) in each chain by the solid-phase method. Two chains were then subjected to the oxidative folding reaction to obtain selenoinsulin. The obtained selenoinsulin assumed quite similar structure with the native insulin and showed similar biological activity. On the other hand, it showed about 10 times higher stability to insulin-degrading enzymes, indicating that it would be useful as a long-lasting insulin drug.

I will then discuss about the synthesis of selenoferredoxin. Ferredoxin is an electron carrier protein, which transfers electrons from photo system I to various ferredoxin dependent enzymes in plant cells. The 2Fe2S cluster supported by four Cys residues are engaged in this process. To analyze the effect of Cys to Sec substitution, we synthesized selenoferredoxin, in which the four Cys residues were substituted with Sec, by the thioester method [5]. The result of the synthesis and its activity measurement will be shown.

Finally, the synthesis and its functional analysis of Sec-substituted epidermal growth factor will be discussed.

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