Laboratory of Protein Organic Chemistry

Institute for Protein Research

Professor	Hironobu HOJO	hojo @protein.osaka-u.ac.jp
Assistant Professor	Toshiki Takei	toshiki.takei @protein.osaka-u.ac.jp
Assistant Professor	Shun ITO	ito @protein.osaka-u.ac.jp

URL: http://www.protein.osaka-u.ac.jp/organic/

Chemical methods enable the synthesis of proteins, which can not be prepared by the recombinant method, such as site-specifically labeled, glycosylated and phosphorylated proteins. Laboratory of Protein Organic Chemistry is aiming to promote new protein researches using these synthetic proteins. Thus, our laboratory is developing facile methods for protein synthesis based on ligation chemistries. The following is a list of specific research projects that we are currently conducting.

Development of efficient protein synthesis methods

Since the development of our chemical protein synthesis method using peptide thioesters in 1991, peptide thioester has been the key intermediate for protein synthesis. Therefore, the development of efficient methods for synthesizing peptide thioesters under mild conditions is being pursued around the world. Our group has also developed unique methods to obtain peptide thioesters using the post-synthetic acyl transfer reactions and further optimization of the methods are being made. We are also developing efficient condensation methods (ligation methods) to connect peptide thioesters sequentially without purification to obtain proteins (Fig. 1). Using these methods, we are conducting research on the synthesis and functional analysis of the following proteins.

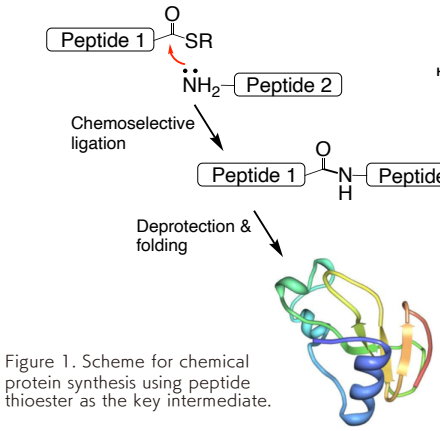

Figure 1. Scheme for chemical protein synthesis using peptide thioester as the key intermediate.

Synthesis of post-translationally modified proteins

Many proteins receives various modifications after translation to function precisely. These post-translationally modification include glycosylation, phosphorylation, methylation, acylation and so on. As for glycosylation, the glycan chains of glycoproteins are highly heterogeneous, which makes the functional and structural studies of glycoprotein difficult. Therefore, we are extending the above ligation chemistry to synthesize glycoproteins with homogeneous glycan chain to elucidate their Recently, we succeeded in the total synthesis of human interleukin-2, which is important for pharmaceutical purposes (Fig. 2). . It is now possible to produce protein drugs by chemical synthesis.

Another post-translational modification is histone modification. It is widely known that gene expression is regulated by acetylation and methylation of histones. However, the exact relationship between modification patterns and gene expression regulation is unknown. Therefore, we have chemically synthesized a series of modified histones and use them to elucidate the correlation between modifications and regulation of gene expression. We are now working to synthesize full-length modified histones and to elucidate their biological significance.

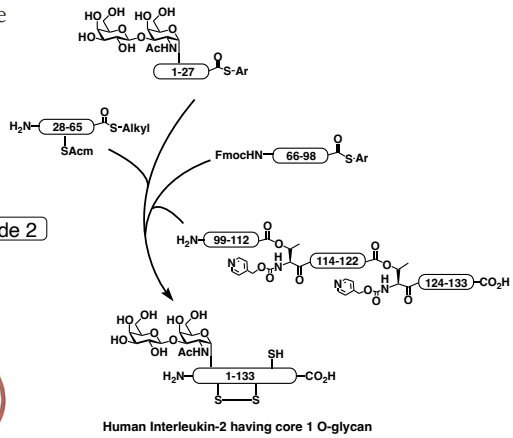

Figure 2. Synthetic route of human interleukin-2.

Development of synthetic methods for membrane proteins and their application to elucidating membrane protein functions

Proteins with transmembrane domains are involved in higher-order biological phenomena such as hormone receptors and ion channels. Therefore, they are not only key substances for understanding life phenomena, but also interesting research targets from the viewpoint of drug development. In our laboratory, we are further extending the above-mentioned methods to efficiently synthesize membrane proteins. A major problem in membrane protein synthesis is that they are highly hydrophobic because they are embedded in lipid bilayers. This makes the polypeptide chains insoluble at various stages of chemical synthesis, causing problems such as inability to ligate peptide segments and inability to purify them. Therefore, we are developing new methods to solubilize polypeptide chains and achieve total synthesis of membrane proteins. (Figure 3)

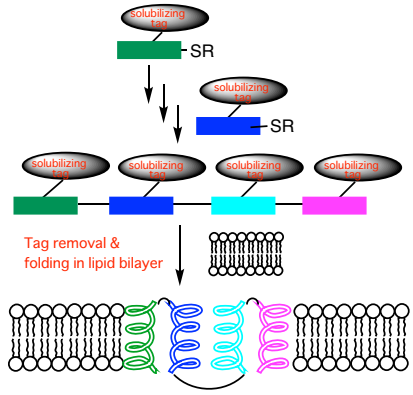

Figure 3. Synthesis of membrane protein.

It is a molecular-level craft. If you like making things, you'll be hooked.

Institute for Protein Research, Osaka University
3-2 Yamadaoka, Suita, Osaka 565-0871, Japan
TEL: +81-6-6879-8601
FAX : +81-6-6879-8603

Scan here for the lab's website >>