August 19, 2008

# Development of a hybrid enzyme that incorporates a non-natural amino acid into proteins

*A mutant tyrosyl-tRNA synthetase was successfully engineered to exhibit strict specificity for a non-natural amino acid*

Proteins play various roles within organisms, giving birth and shape to new life, assisting development, and transmitting genetic information over generations. Protein molecules are composed of only 20 types of amino acids, the composition and order of which define the structure and function of the protein. This fundamental characteristic suggests that an increase in the number of amino-acid types should enable the creation of novel proteins to meet human needs. Recent years have witnessed some progress in the incorporation of non-natural amino acids (amino acids not found in nature) into proteins with novel, artificial properties.

Proteins are synthesized according to genetic information, and certain proteins help the genetic contents to be interpreted precisely. Engineering the properties of these proteins that mediate this fundamental life process is generally considered to be difficult. Collaborative research by RIKEN and the University of Tokyo, however, has generated from one of these proteins a novel, hybrid enzyme which can interpret the genetic information in such a manner that non-natural amino acid is incorporated into proteins. This hybrid enzyme has two active sites originating from different proteins, each from a distinct organism, and is able to precisely select iodinated tyrosine (iodotyrosine) as an amino acid to be incorporated into proteins. One active site attaches the iodotyrosine to tRNA, and the other removes the amino acids from tRNA that happen to attach the wrong amino acids. This hybrid enzyme has successfully achieved biosynthesis of proteins containing iodotyrosine at desired positions.

The successful development of novel, hybrid enzymes will lead to the large-scale production of various useful proteins containing non-natural amino acids, including proteins serving as highly effective therapeutic agents, enzymes with drastically improved activities, and bio-materials for industrial uses.

**Original work:**

Kenji Oki , Kensaku Sakamoto, Takatsugu Kobayashi, Hiroshi M. Sasaki, and Shigeyuki Yokoyama

Transplantation of a tyrosine editing domain into a tyrosyl-tRNA synthetase variant enhances its specificity for a tyrosine analog

Proc Natl Acad Sci U S A. 2008 Sep 16;105(37):13699-700.

PubMed

For more information, please contact:

RIKEN Public Relations Office

Email: koho@riken.jp