

2nd International Conference on

Systems & Synthetic Biology

August 18-20, 2016 London, UK

Use of synthetic proteins and future trends: The example of calstabin

Jean A Boutin

Institut de recherches SERVIER, France

Synthetic biology is a growing field in which the contribution brought by chemical synthesis of proteins and particularly enzymes is fundamental. Despite this fact, the chemical synthesis of catalytic active proteins remains poorly documented, essentially because it is hard to obtain enough material to use it in biochemical experiments. Chemical synthesis of proteins could permit to have access to the incorporation of unnatural (exotic) amino acids into catalytic active proteins, a feature amenable by recombinant technologies, but that requires delicate manipulation of the bacterial machinery. The developments brought by this approach, include but are not limited to the measure of the influence of unnatural (exotic) amino acids on the 3D structure of enzyme, its activity as well as their recognition of substrate, co-substrate or regulator. The main limitation remains a quantitative problem: How to progress from microgram of proteins produced nowadays with essentially recombinant techniques to tens of milligrams? We chose to present as a model the synthesis and thorough characterization of calstabin, a short protein proline isomerase of 107 amino acids. The protein was synthesized using the native chemical ligation approach. Several tens of milligrams were obtained. Therefore, we were able to refold the polypeptide properly, to characterize its biophysical properties, to measure its catalytic activity and finally to crystallize it in order to obtain its tridimensional structure after X-ray diffraction. Further to it and as a first step of validation of the whole process, we incorporated exotic amino acids in the easiest reachable part of the protein N-terminus. Avenues are now open to obtain further proteins modified with exotic amino acids in a way that is only barely accessible by molecular biology. We hope that these approaches will permit to gain detailed information on the structure-function relationship of proteins as long as they are reachable by complete chemical synthesis (below 300 amino acids).

Biography

Jean A Boutin graduated (Thèse d'Etat en Sciences Biologiques) from Nancy University (France) on drug metabolism. He did his postdoctoral training at Johns Hopkins (Baltimore) and at the Karolinska Institutet (Stockholm, Sweden). He was hired as protein chemist in Les Laboratoires SERVIER (LLS) in 1986. During the 30ish last years, Dr. Boutin moved from oncology to peptide research and then molecular & cellular pharmacology. Recently, LLS created a drug discovery platform that Dr. Boutin leads. This structure involves all the aspects of drug discovery, from molecular modeling to ligand/protein biophysical interaction measurements, including protein chemistry, stem cells, structural biology, chemogenetics, HTS, biophysics, Biologics. The main interests of Dr. Boutin are N-myristoyltransferase, melatonin, quinone reductase 2, MCH and autotaxin. In relation with Biologics, our group more particularly explores all the areas related to the possibilities to incorporate exotic amino acids into proteins, especially enzymes.

jean.boutin@servier.com

Notes: