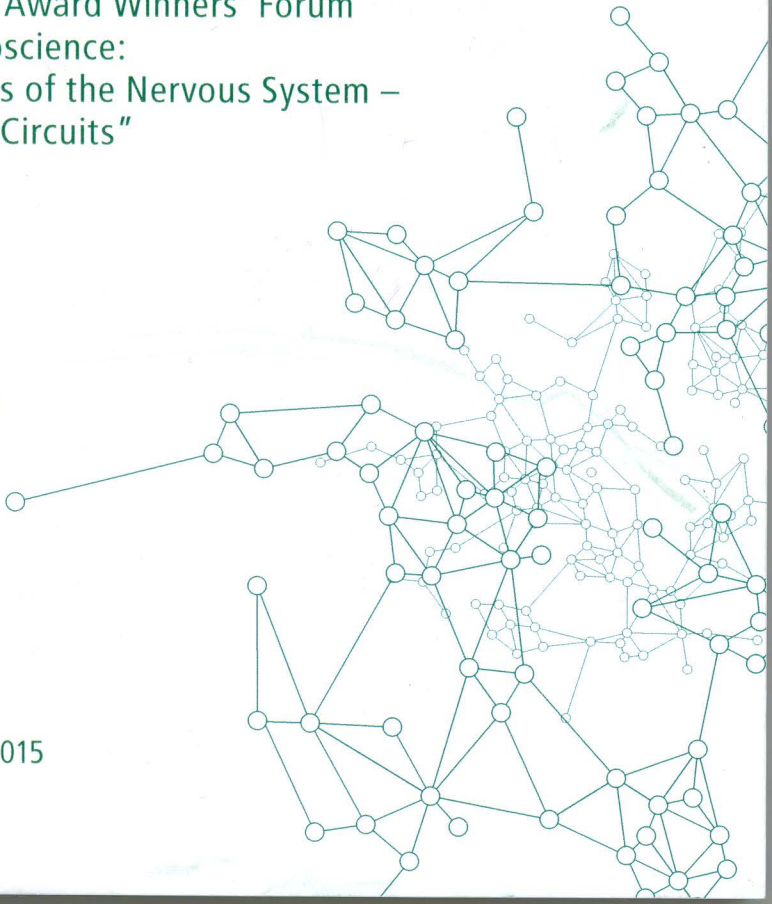
Alexander von Humboldt
Stiftung/Foundation

Networking Guide

5th Bonn Humboldt Award Winners' Forum "Frontiers in Neuroscience: Multi-Scale Analysis of the Nervous System – From Molecules to Circuits"



Bonn, 7 - 10 October 2015

Table of Contents:

Vladimir I. Tishkov
Moscow M.V. Lomonosov State University
Russian Federation

Moscow M.V. Lomonosov State University
Faculty of Chemistry
Department of Chemical Enzymology
Leninskie Gory, 1-3
119991 Moscow
Russian Federation

vitishkov@gmail.com

Discipline
Biochemistry

Keywords
Biochemistry, Biomolecules Structure, Biotechnology, Enzymology, Genetic Engineering

D-amino acid oxidase as a tool for biotechnology and medicine diagnostics.

D-amino acids (D-Ser, D-Ala, D-Glu etc.) are regulators of many processes in organism including regulation of nervous system. Low level of D-Ser is direct indicator for possible development of schizophrenia (Chumakov et al. PNAS 2002). D-amino acid oxidase (DAAO) is responsible for control of level of D-amino acids in organism. The enzyme can be used in biosensors to determine concentrations of D-amino acids in vivo. The main drawback is wide substrate specificity of native enzyme.

DAAO is also widely used in biotechnology for fine organic (especially chiral) synthesis. For example, it is used in two-enzyme biocatalytic process of preparation of 7-aminocephalosporanic acid (7-ACA) from cephalosporine C (CephC). 7-ACA is main sinton for preparation of semi-synthetis cephalosporins. Unfortunately, native DAAO from yeast Trygonopsis variabilis (TvDAAO) used in the process has not sufficient catalytic activity with CephC as well as thermal and chemical stability.

In our laboratory we cloned gene of TvDAAO and developed highly efficient expression system in E.coli cells. Using rational design approach we prepared more than 60 mutant forms of TvDAAO and succeeded to crystallize one mutant and solved it structure with 1.8 angstrem resolution. Many mutant had higher catalytic efficiency in CephC oxidation, higher thermal and chemical stability. Many amino acid changes resulted in mutant TvDAAO specific to certain D-amino acid. These mutants can be used in biosensors for specific analysis of required D-amino acids in vivo.

Co-Authors:
Svyatoslav Savin

Vita
Date of Birth 09.11.1957
2014 - present - Executive Dean in Science of Chemistry Faculty, M.V.Lomonosov Moscow State University
1998 - present - Professor, M.V.Lomonosov Moscow State University
2008 - present - Head of Lab of Molecular Engineering, A.N.Bach Institute of Biochemistry, Russian Academy of Sciences