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Biography

Oleg Melnyk graduated as an engineer in chemistry in 1989 from the Ecole Nationale de Chimie de Paris (ENSCP, France). He received his Ph.D. degree in 1994 from the University of Paris VI (France). During his thesis work, he developed a semisynthetic route to cortisone. After post-doctoral training from 1994 to 1996 in the group of Prof. A. Tartar (Lille, France) he was recruited by the Centre National de la Recherche Scientifique (CNRS) in Lille. He is now director of research at CNRS and his main research interests are the development of chemical methods for protein synthesis and the study of protein function.

Abstract title: A cysteine selenosulfide redox switch for protein chemical synthesis

Abstract

The control of cysteine reactivity is of paramount importance for the synthesis of proteins using the native chemical ligation (NCL) reaction. We discovered that this goal can be achieved in a traceless manner during ligation by appending a simple *N*-selenoethyl group to cysteine. While in synthetic organic chemistry the cleavage of carbon-nitrogen bonds is notoriously difficult, we found that *N*-selenoethyl cysteine (SetCys) loses its selenoethyl arm in water under mild conditions upon reduction of its selenosulfide bond. Detailed mechanistic investigations uncover a novel mode of reactivity for Cys. Its implementation in a process enabling the modular and straightforward assembly of backbone cyclized polypeptides is illustrated by the synthesis of biologically active cyclic hepatocyte growth factor mimics.