Research Doctorate (Ph.D.) in Chemical Sciences
33rd Cycle – Academic Year 2017/2018

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Project Information

1. Title

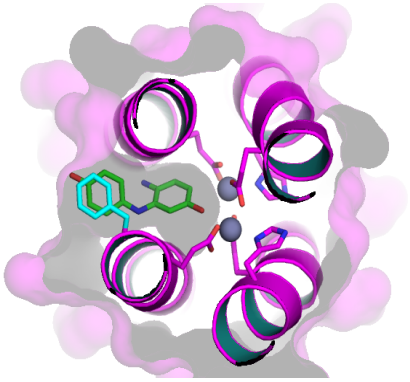
Beyond the functions of natural metalloenzymes: *de novo* designed biocatalysts for non-natural transformations.

2. Key words

Entirely artificial metalloenzymes; "biologically unavailable" metal cofactors; protein design; non-natural transformations; structural and functional characterization.

3. Abstract

The engineering of biocatalysts that expand the repertoire of reactions catalyzed by Nature has a great impact in chemical and biotech industries. In the last years, two main methodologies have been adopted: *i) de novo* design of enzymes, which stabilize the transition state of a target reaction; *ii)* engineering of natural proteins with metal-based homogeneous catalysts. The goal of the present project is to overcome these two methodologies by developing entirely artificial metalloenzymes. To this aim, sites for hosting homogeneous catalysts will be carved within *de novo* designed protein scaffolds. In particular, exploiting our expertise in the development of DF (Due Ferri) proteins, *de novo* proteins will be designed to bind and activate metals in the "biologically unavailable" parts of the periodic table. Their catalytic activity will be studied, paying attention to their kinetic parameters, regio- and stereospecificities, and substrate scope.



Refined docking model of Zn^{II}-DF-C1 and the interacting intermediate.