3èmes Journées
de Catalyse de Paris Saclay
5-6 avril 2018
Auditorium IMAGIF, Centre de Recherches de Gif-sur-Yvette

Receptor-based artificial metalloenzymes on human cells

W. Ghattas, V. Dubosclard, A. Wick, R. Guillot, R. Ricoux, J-P. Mahy

Institut de Chimie Moléculaire et des Matériaux d'Orsay, ICMMO UMR8182
Univerisité Paris-Saclay, Bât. 420 rue du doyen Georges Poitou 91405 cedex Orsay
Wadih.ghattas@u-psud.fr

Artificial metalloenzymes (AM) are prepared by incorporating synthetic transition metal catalysts into host proteins.[1] These hybrid biocatalysts are imparted with extraordinary catalytic properties provided by the metal cofactor and with a protective and stereoselective environment provided by the protein. They constitute thus powerful tools to expand the repertoire of reactions catalyzed by natural enzymes. The preparation of such AM could also be envisioned *in vivo* in selected organs by using metal cofactors that target host proteins and by avoiding the deactivation of the metal cofactor caused by cellular components.[2]

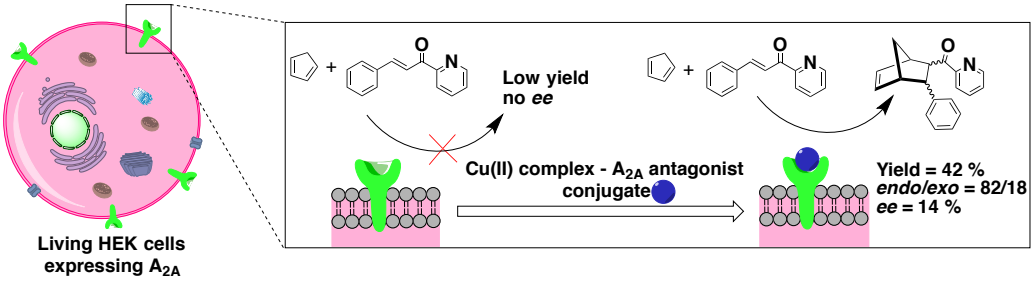

Figure 1: Catalysis of a Diels-Alder cycloaddition by an artificial enzyme built using the A_{2A} receptor and a Cu(II) cofactor.

In this context, we developed an original approach to build up AM at the surface of living Human Embryonic Kidney (HEK) cells, hence using human cell membranes as a compartment to shield metal cofactors from damage. Our strategy targeted the wild type human A_{2A} Adenosine Receptor by incorporating in its binding site a conjugate of one of its strong antagonists covalently bound to a copper(II) catalyst. To our knowledge, membrane receptors were never used to form artificial enzymes thus far. The catalytic potential of the receptor based artificial metalloenzyme was evaluated in a prototype-reaction *i.e.* the Diels-Alder cycloaddition reaction, a carbon-carbon bond forming reaction that is not catalyzed by any known human enzyme. The characteristics of this reaction, *i.e.* yield and stereoselectivity,[3] were in line with those expected for an enzyme catalysed reaction (Fig. 1), which was further corroborated by similar findings we obtained using the purified receptor-based artificial enzyme.

References

1. F. Schwizer, T. R. Ward and coll. , *Chem. Rev.* **2018**, *118*, 142.
2. E. M. Sletten, C. R. Bertozzi, C. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 6974.
3. W. Ghattas et al., *J. Am. Chem. Soc.* in revision.