

# Supramolecular Engineered Nanobiocatalysts Capable of Asymmetric Catalysis in Organic Solvents [NanoBioCat]

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## Project Summary

A large number of high-value specialty chemicals and active pharmaceutical ingredients (APIs) are asymmetric; they are preferably produced as pure enantiomers. A large number of chemical asymmetric catalysts have been developed. However, the level of enantioselectivity of the reaction reached is always lower than that of natural or engineered enzymes.

In this context, enzymes have a pivotal importance as they are potent natural catalysts that can operate under mild conditions and often display high chemo-, regio- and stereoselectivity, elevated turnover rates, and often good substrate selectivity. Enzymes are therefore first-choice candidates for asymmetric synthesis. However, the use of the majority of natural enzymes is mainly limited to aqueous solvents in which many specialty chemicals are not or poorly soluble.

The *NanoBioCat* project builds upon recent results acquired by the proposers in nanobiocatalysts design;<sup>1-3</sup> it aims at developing stable nanobiocatalysts capable of asymmetric catalysis and cofactor regeneration in organic solvents.

In more details, the nanobiocatalysts will be designed so that two different enzymes are immobilized and shielded by a protection layer at the surface of mesoporous silica nanoparticles. In the aqueous nano-environment of the nanoparticle, the first enzyme will catalyze an asymmetric reductive amination on a apolar substrate molecule diffusing through the protection layer and concomitantly consume a reduced cofactor molecule (NADPH,H+).

<sup>1</sup>. Correro, M. R.; Moridi, N.; Schutzinger, H.; Sykora, S.; Ammann, E. M.; Peters, E. H.; Dudal, Y.; Corvini, P. F.; Shahgaldian, P., Enzyme Shielding in an Enzyme-thin and Soft Organosilica Layer. *Angew. Chem., Int. Ed.* **2016**, *55* (21), 6285-9.

<sup>2</sup>. Hesticova, M.; Correro, M. R.; Lenz, M.; Corvini, P. F.; Shahgaldian, P.; Ward, T. R., Immobilization of an artificial imine reductase within silica nanoparticles improves its performance. *Chem. Commun.* **2016**, *52* (60), 9462-5.

<sup>3</sup>. Correro, M. R.; Sykora, S.; Corvini, P. F.; Shahgaldian, P., Enzyme Armoring by an Organosilica Layer: Synthesis and Characterization of Hybrid Organic/Inorganic Nanobiocatalysts. *Methods Enzymol.* **2017**, *590*, 77-91.

<sup>4</sup>. Aleku, G. A.; France, S. P.; Man, H.; Mangas-Sanchez, J.; Montgomery, S. L.; Sharma, M.; Leipold, F.; Hussain, S.; Grogan, G.; Turner, N. J., A reductive aminase from *Aspergillus oryzae*. *Nat. Chem.* **2017**, doi:10.1038/nchem.2782.