

CELSA

Central Europe Leuven Strategic Alliance

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## **CELSA - Collaborative research project - Application form - COVER PAGE**

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**3. Non confidential and public friendly summary (max. 2000 characters)**

**Project title:** Concerto for solids and biocatalysts - Cascade biocatalysis and heterogeneous catalysis for fine chemicals production (**ConSolid**)

**Summary:**

Complex pharmaceuticals often have the desired medical effect only in one ‘enantiomeric’ form, while the mirror image may have no or even adverse effects. Biocatalysts like enzymes often succeed to transform selectively 1 of the 2 enantiomers of a precursor to a desired product, a process termed ‘Kinetic Resolution’ (KR). To valorize the remaining 50% of ‘wrong’ enantiomer in the initial 50-50 ‘racemate’, a racemization catalyst must be added, which can interconvert the 2 enantiomers. The overall process, with combined biocatalyst and chemical racemization catalyst, is known as ‘Dynamic Kinetic Resolution’ (DKR); it works well for alcohols, but has met with limited success for the important amines and (non-natural) amino acids. Here we aim at large steps forward in the enantiopure synthesis of amines and amino acids by producing and integrating new racemization catalysts and biocatalysts. First, new Ru- and Ni-based catalysts, or metal-organic framework catalysts will be designed (at KULeuven) for the racemization of aliphatic amines. These should foremost be compatible with the enzymes, avoiding e.g. poisoning of the enzymes by leached metals. Secondly, next to the known hydrolases used for amine KR, we will innovate the range of enzymes that can be applied in DKR, focusing on enzymes using the MIO cofactor for amine transformations, e.g. phenylalanine 2,3-aminomutases (PAM) (at BME). Innovative schemes integrating MIO-enzymes in DKR are proposed.

Summarizing, solid racemization catalysts (Leuven) and immobilized biocatalysts (Budapest) will physically meet in one (tubular) reactor, allowing the full DKR, with production of enantiopure compounds in high yields. The expertise of Budapest in continuous-flow enzymatic reactions will bring the process to practical reality. The selected reactions aim at important chiral amines (precursors to active pharmaceutical ingredients) and non-natural  $\alpha$ - or  $\beta$ -amino acids (building blocks for peptide drugs).

**4. List 5 key words**

Sustainable chemistry; Solid racemization catalysts; Biocatalysis; Fine chemicals; Continuous-flow process