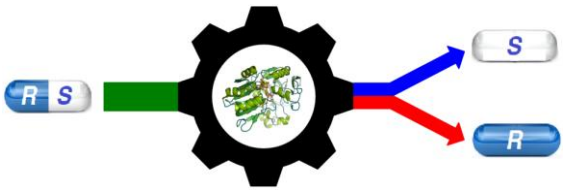
Nowadays, developing of new, cost-efficient and sustainable methodologies for active pharmaceuticals ingredients (APIs) manufacturing is of prime concern not only for academia and pharmaceutical industry, but especially for high-quality drugs and ensuring patient safety. Moreover, chiral APIs are present in over 80% of drugs currently on the market, and therefore, their production in optically pure form is of paramount importance for the target-oriented therapies. Notably, especially when the pharmacological activity resides mainly in one of the stereoisomers, then enantiomeric drugs are superior to the racemates as they are characterized by an improved therapeutic index being a result of increased potency and selectivity in action as well as decreased side-effects. Moreover, the advantages of using single-stereoisomeric APIs is that they exhibit both a faster onset of action and diminution in propensity for drug-drug interactions as well as possess the potential to provide the exposition of the patient to a lower dosage. In this context, biocatalysis offers clear advantages for innovative manufacturing processes of biologically active chiral molecules as it enables asymmetric synthesis of single enantiomers in a much simpler and efficient manner than synthetic chemical methods. This stems mostly from the fact that in order to respond to external stimuli and regulate internal states *in vivo* enzymes evolved over billions of years into extremely efficient catalysts that initiates and accelerates biochemical reactions with unmatched chemo-, regio-, and stereo-selectivity. Furthermore, biocatalysis posses ability to operate under mild neutral conditions, encompass a reduced environmental footprint, and thus deliver the products at significantly lower cost level within improved safety regimes what all together place it definitely among the most relevant branches of '*the 12 Principles of Green Chemistry*' formulated by P. Anastas and J. Warner. Moreover, various engineering concepts including protein engineering in the context of so-called 'Directed Enzyme Evolution' (the Nobel Prize in Chemistry 2018 was awarded to Prof. F. H. Arnold), substrate engineering, medium engineering, biocatalyst (formulation) engineering and/or reactor engineering have consequently moved this scientific discipline from academic avant-garde to an industrially attractive technology. In addition, new strategies for increasing the level of biocatalysis' efficiency and applicability, such as development of: (i) (chemo)multienzymatic cascades, (ii) biocatalytic multi-enzyme fusion systems, and (iii) nature-inspired enzyme-based artificial metabolic pathways consisting of complex reaction networks have opened extraordinary opportunities not only for fundamental science purposes/discoveries but also for industrial application. Remarkably, over the last decades biocatalytic methods have emerged as an indispensable and versatile tool for the asymmetric synthesis of high-value optically pure compounds, and especially, small-molecule APIs. In this regard, excellent properties displayed by hydrolases and oxidoreducatases in terms of sophisticated selectivity and remarkable catalytic activity toward broad range of xenobiotics make them the most exploited group of biocatalysts in the synthesis of enantiomerically enriched compounds including pharmaceuticals and their intermediates. Moreover, among those enzymes, i.e. lipases posses great ability to catalyze transformations of wide range of structurally different substrates in low-water environments and without addition of expensive cofactors. Therefore, it is not surprising that lipase-based transformations, possible to be conducted in neat organic solvents, outperforms other biocatalytic systems composed of different enzymes, and thus may still constitute a foundation for emerging technologies and strategies for chemoenzymatic synthesis of generic versions of established chiral drugs.



The major aim of this Project is to elaborate novel chemoenzymatic methodologies toward preparation of non-racemic pharmaceuticals by employing hydrolytic and/or oxidoreductive enzymes as the catalysts for the key asymmetric transformations. In this regard, the major research challenges will be aimed at development of lipase-catalyzed chromatography-free kinetic resolution (KR) approach toward racemic *sec*-alcohols using novel acyl donors as well as highly efficient transition-metal-free dynamic kinetic resolution (DKR) methodology designed on the basis of bi-catalytic systems composed of lipases and nano-sized heterogeneous 'super acidic' catalysts. Moreover, studies on the sequential one-pot two-step oxidation-reduction deracemization of *sec*-alcohols catalyzed by (laccase/TEMPO)-ketoreductase will also be applied in respect to extending the reaction toolbox for asymmetric synthesis of chiral building blocks. It is worth noting that alcohol deracemization reactions will be carried out using recombinant enzymes prepared in the framework of international cooperation with scientists from the University of Graz. All the designed enzymatic methods will be optimized with regard to reaction yields and enantioselectivity as well as fully characterized in terms of stereochemical outcome. It is expected that the designed enzymatic protocols, mostly due to their simplicity and high catalytic efficiency, would become a great alternative towards currently used synthetic methods and will draw an attention of pharma industry in the future.