

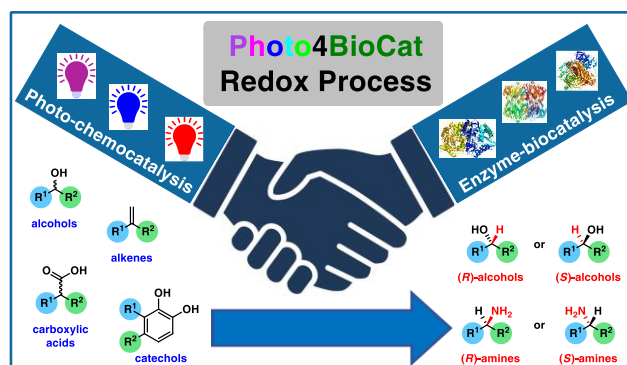
Nature has always been a source of constant inspiration for chemists, not only because of the enormous variety of chemical compounds that living organisms can produce but also because of the extraordinary biosynthetic strategies used to obtain them. These natural, biosynthetic strategies are based on the use of enzymes as catalysts of crucial chemical transformations, the compartmentalization of enzymes or even entire biosynthetic pathways in cellular organelles, and the sequential use of enzymes in complex metabolic pathways that allow living beings to build complex molecules from simple building blocks.

Leveraging the power of nature for sustainable chemical synthesis is of prime importance for academia and industry since utilizing enzymes as biocatalysts in chemical reactions can significantly accelerate product formation under mild reaction conditions (i.e., ambient temperature, normal pressure, neutral pH, etc.), and transform the respective organic substrates with excellent chemo-, regio-, and stereoselectivity while preserving the requirements of environmental benignity. Therefore, enzymes have become an ingenious tool for building chiral molecules in a highly efficient, straightforward, and selective fashion, which often drastically outperforms the catalytic potential of both transition-metal catalysts and organocatalysts. Incorporating enzymes into technologies can dramatically shorten the synthetic pathways, leading to less toxic waste generation and improved cost-efficiency. Moreover, recent years have seen great efforts in mimicking the metabolism of living organisms by combining several types of enzymes in a single reaction vessel to obtain complex molecules without isolating intermediates. Such artificial 'one-pot' biocatalytic cascade reactions using hybrid biotechnological systems have opened new avenues for challenging synthetic endeavors, especially for the manufacturing of chiral drugs, in which chemical and optical purity of active pharmaceutical ingredients (APIs) are the paramount factors of therapeutic activity and safety of usage.

In turn, no life on Earth could be possible without solar light! Except for the well-known crucial functions of sunlight in such fundamental biochemical processes as photosynthesis in plants and cyanobacteria, or production of vitamin D₃ and melanin in mammalian skin, or the secretion of hormones (i.e., serotonin, melatonin) in the pineal gland and brain of human beings, the solar electromagnetic radiation is also expected to play an essential role in origins of the chiral nature of basic building blocks of life, such as amino acids and carbohydrates. Inspired by these revelations, chemists have researched the streamlining of chemical processes with UV or visible light irradiation for decades. In this context, the developments of the last few years showed the enormous potential of using especially blue light as a "clean and safe" alternative energy source and a plethora of photocatalysts for their ability to facilitate a range of chemical transformations with an impressive outcome. Moreover, the phenomenon of the light-driven processes lies in a wealth of new chemical reactivities; thus, photo-chemocatalysis represents a unique synthetic toolbox for organic chemists to accomplish a host of challenging transformations not achievable with conventional chemo- and biocatalysis.

Hence, the ultimate goal of this Project's proposal is to develop a novel, practical, eco-friendly, and ultra-efficient (in terms of products' yield and reactions' stereoselectivity) solar-driven biocatalytic reaction platform for deracemization of chiral compounds or valorization of waste organic molecules into high-value-added products (i.e., alcohols, amines, etc.) useful as building blocks in the pharmaceutical industry. This task will be achieved

by employing various racemic compounds (i.e., *sec*-alcohols, carboxylic acids, etc.), alkenes, or catechols as substrates and the combination of photocatalysis and redox biotransformations, including chemoenzymatic oxyfunctionalization of C–O bonds, bio-*trans*-hydrogenation and/or reductive amination of C=O bonds, and enantioselective transformation of racemic alcohols. As illustrated in the graphical abstract, the elaborated one-pot photo-biocatalytic systems and multi-enzymatic cascades will comprise visible light (from purple-390 nm to red-630 nm) as



the source of electromagnetic irradiation and a set of standard commercially available or newly discovered photocatalysts coupled with the library of wild-type and engineered variants of recombinant enzymes from different classes, including oxidoreductases [i.e., alcohol dehydrogenases (ADHs), catalases], transferases [i.e., transaminases (TAs), acyltransferases (MsAcTs)], oxidases (laccases, aldehyde oxidases), and hydrolases (lipases), respectively. **All the biocatalysts mentioned above will be prepared in collaboration with Prof. Wolfgang Kroutil from the University of Graz.** A key aspect of the research will be focused on optimizing the photo-biocatalytic conditions so that compatibility and synergy between the processes mentioned above are preserved, thus enabling the achievement of desired catalytic activity of both photo- and biocatalysts. It is expected that the designed photo-enzymatic procedures for the synthesis of optically pure compounds, due to their simplicity and high catalytic efficiency, will become an excellent alternative to the currently used synthetic methods and will be applied in the pharmaceutical industry to produce innovative drugs in the future.