COMPUTER-AIDED ENGINEERING OF ENZYMES FOR *IN VITRO* AND *IN VIVO* PRODUCTION OF NOVEL PRECURSORS

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Development of enzyme-based synthetic processes is often hampered by the lack of natural enzymes with requisite properties or specificities. With the potential offered nowadays by computer-aided molecular design and enzyme engineering techniques, we have seen in recent years numerous examples of successful enzyme designs that enabled tremendous improvements of catalytic properties for various applications, including catalysis of novel synthetic reactions. Nonetheless, progress in this field, in particular with computational techniques, is still required in order to fasten enzyme design and accelerate the generation of efficient biocatalysts.

This lecture will report and discuss recent developments and specific research projects of our laboratory. Special emphasis will be placed on the contribution of computational methods in our strategies.
Several areas will be covered: (i) development of computational methods for multi-scale molecular modelling and design inspired from artificial intelligence field [1-2]; (ii) computer-aided engineering of carbohydrate-active enzymes to conceive catalysts acting on non-natural substrates, chemically protected to integrate programmed chemo-enzymatic cascades, and ultimately produce antigenic oligosaccharide precursors [3-5]; (iii) structure - based engineering of enzymes to conceive an artificial metabolic pathway dedicated to *in vivo* production of non-natural methionine precursor 2,4-Dihydroxybutyric acid (DHB) [6].

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