Biotransformation of inexpensive natural platform chemicals to higher value flavor compounds

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The project focuses on biotranformations of relative inexpensive natural platform chemicals derived from distillation of essential oils and non-volatile compounds to higher value flavour compounds through biocatalysis. Experimental processes using a range of enzymes (cytochrome P450s, aldo-keto reductases/alcohol dehydrogenases and carotenoid cleavage oxygenases) from various sources have been previously described and a number of high value flavour components produced from inexpensive starting materials. In this project similar processes will be used to transform platform molecules using an array of enzymes focussed around those previously described.

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Different structure-oriented design of selective butyrylcholinesterase probe and its application in drug discovery

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The two major human cholinesterases are acetylcholinesterase (AChE; EC 3.1.1.7) and butyrylcholinesterase (BChE; EC 3.1.1.8), and are very important enzymes in multiple areas such as pharmacology, neurobiology and toxicology due to their significant roles in human body and health. Although the biological function is uncertain, the BChE levels have been implicated in lipid metabolism and various human diseases such as liver damage, cirrhosis, Alzheimer's disease (AD) and liver metastasis. BChE is also responsible for detoxifying xenobiotics like organophosphates and cocaine and is a well-known biomarker for clinical diagnosis. Thus, the quantification of BChE activity and its inhibition is not only important in diseases diagnosis, but also indispensable for drug discovery. We report on the different structure-oriented design and application of a selective fluorogenic molecular probe (BChE-FP) for human butyrylcholinesterase (BChE). This probe, rationally designed by mimicking the native substrate and manipulating the steric feature of the recognition group of designed probes targeting the structural difference of the active sites for BChE and acetylcholinesterase (AChE), exhibits near-zero background fluorescence but produce remarkable fluorescence enhancement upon the catalysis by BChE in a fast biochemical reaction. To the best of our knowledge, BChE-FP is the first probe that can discriminate BChE from AChE, which is successfully applied for BChE inhibitor screening and characterization under physiological conditions, and BChE detection in human serum. These results demonstrate that this molecular probe can function as a useful molecular tool for high-throughput drug discovery against BChE-related diseases, as well as the biosensing for neuromuscular blocking agents.

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