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Extending the reaction toolbox for C-C bond formation and cleavage: biocatalytic applications of Transketolase

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Abstract

Over 70% of women with breast cancer are with hormone receptor positive disease [1], and most of them are treated with an adjuvant endocrine therapy. Five years tamoxifen used to be a standard adjuvant endocrine treatment of breast cancer. It was shown by a metaanalysis that tamoxifen reduced about 40% of recurrence rates in both premenopausal and postmenopausal women with breast cancer [2]. Third generation Aromatase Inhibitors (AIs), exemestane (steroidal), anastrozole (non-steroidal), and letrozole (non-steroidal) began to be used in late 90's as an adjuvant endocrine therapy in postmenopausal women with breast cancer. A randomized controlled trial showed that 5 years adjuvant anastrozole was superior to 5 years adjuvant tamoxifen in terms of disease-free survival (DFS) rates [3]. In addition another randomized controlled trial showed that 5 years of adjuvant letrozole was superior to 5 years adjuvant tamoxifen in terms of DFS rates and overall survival (OS) rates [4]. .

Biography:

Laurence Hecquet (Full Professor since 2000, PhD) develops her research activities at the Institute of chemistry of Clermont-Ferrand (ICCF, UMR 6296), University Clermont Auvergne (UCA), France. Her research focuses on the enzymatic synthesis of chiral compounds particularly by stereoselective carboligation catalyzed by transketolase (TK), a thiamine diphosphate (ThDP) dependent enzyme. Her group has recently discovered and engineered by directed evolution a novel thermostable TK from Geobacillus stearothermophilus. The best TK variants efficiently improved wild type TK activity toward pyruvate and higher aliphatic homologues as nucleophiles and toward a large range of polyhydroxylated or aliphatic aldehydes as electophiles. The biocatalytic applications led to various chiral hydroxyketones with high stereocontrol. The long-term goals of her works are to broaden the substrate spectra of TK and of other ThDP enzymes and to optimize the biocatalytic processes in developping multienzymatic cascade reaction.

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