MEETING ABSTRACTS

NEW PROGRESS IN DRUG DESIGN, DISCOVERY AND DEVELOPMENT INVOLVING CHOLINESTERASES

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This talk will briefly discuss our newest progress in drug design, discovery and development involving cholinesterases, particularly in three major therapeutic areas.

(1) On the basis of our previous design and discovery of cocaine hydrolases (CocHs) engineered from human butyrylcholinesterase (BChE), we have further developed a novel, long-acting CocH form, and demonstrated the promising clinical potential of CocHs for therapeutic treatment of cocaine overdose and addiction in clinically relevant animal models. One of the long-acting CocHs is currently in the large-scale protein drug manufacturing process development.

(2) It has been demonstrated that a long-acting CocH (enzyme) is capable of both completely blocking cocaine-induced physiological effects and producing the desirable anti-obesity effects. Mice on a high-fat diet gained significantly less body weight when treated weekly with 1 mg/kg enzyme compared to control mice.

(3) Most recently, we have also designed and tested a new therapeutic strategy for heroin detoxification based on a detailed analysis of the cholinesterases-involved chemical transformation and functional change of heroin in the body. It has been demonstrated in our animal models that a carefully selected cholinesterase inhibitor attenuated acute toxicity and physiological effects of heroin, whereas some other cholinesterase inhibitors may actually enhance the acute toxicity and physiological effects of heroin.