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TOPIC(s) : Enzyme discovery and engineering

Turning a hyperthermostable lactonase into a proficient phosphotriesterase for the decontamination of organophosphorus chemicals

AUTHORS

Pauline JACQUET / GENE&GREENTK, 19-21 BOULEVARD JEAN MOULIN, MARSEILLE
David DAUDÉ / GENE&GREENTK, 19-21 BOULEVARD JEAN MOULIN, MARSEILLE
Eric CHABRIÈRE / AIX MARSEILLE UNIV / IHU-MÉDITERRANÉE INFECTION, 19-21 BOULEVARD JEAN MOULIN, MARSEILLE
Mikael ELIAS / UNIVERSITY OF MINNESOTA, 1479 GORTNER AVENUE, SAINT PAUL
Corresponding author : David DAUDÉ / david.daude@gene-greentk.com

PURPOSE OF THE ABSTRACT

Organophosphorus (OP) chemicals are neurotoxic compounds developed as pesticides (such as chlorpyrifos or malathion) and chemical warfare nerve agents (CWNA, such as sarin or VX). These compounds are responsible of worldwide pollution and represent a serious terrorist threat. Developing safe and efficient decontamination strategies against OP poisoning is of outmost interest and OP-degrading enzymes have gained special attention [1].

In that context, we focused on the enzyme SsoPox, a hyperthermostable phosphotriesterase-like lactonase, isolated from the extremophilic archaeon Saccharolobus solfataricus. This enzyme is highly robust and constitutes a promising candidate for engineering strategies. Considering its structural similarities with bacterial phosphotriesterases, SsoPox was engineered for increasing its capacity to degrade OP chemicals. Combinatorial approaches were used to increase catalytic performances and various improved variants were obtained. These variants carried from two to seven mutations and up to 2210-fold improvement were achieved [2,3]. Among these, two variants with tremendous degradation capacity towards OP were further considered for detoxification purposes.

Two animal models were implemented to evaluate the protective effect of SsoPox variants against OP poisoning. Variant SsoPox-αsD6, improved against numerous pesticides (including chlorpyrifos, malathion or diazinon), was able to decrease toxicity and enhance survival in planarian flatworms exposed to acute poisoning and to protect them from long term effects upon chronic exposure [4,5]. This enzyme was further immobilized in a filtration device that may find interest for decontaminating toxic effluents [6]. Another variant, SsoPox-IIIC1, enhanced on ethyl-paraoxon and CWNA analogues, was encapsulated in nanoreactors made of polyethylene glycol–polypropylene sulfide membrane. These nanoreactors containing SsoPox were used to detoxify ethyl-paraoxon in mice in both prophylaxis and post-exposure treatments [7].

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS
Phosphotriesterase | Hyperthermostable | Organophosphorus chemicals | Detoxification

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