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MEETING ABSTRACTS

BORDERLINE BETWEEN CATALYTIC AND NON-CATALYTIC BIO SCAVENGERS: THE EXAMPLE OF ALBUMIN AND REVERSIBLE B-ESTERASES

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Protective mechanism against organophosphorus compounds (OPs) toxicity are mainly based in molecular processes frequently divided conceptually in (A) catalytic and (B) non-catalytic bio-scavengers. Modified natural proteins and small molecules have been developed for applying in therapy and protection. The catalytic ones are mainly associate to the classical concept of A-esterases (phosphotriesterases, PTEs, i.e. paraoxonase); they hydrolyze carboxylesters and OPs by a divalent cation dependent mechanism. The non-catalytic scavengers are mainly associated to covalent binding to proteins, especially B-esterases with a serine or tyrosine residue, which hydrolyzes carboxylesters. However, if an OP is bound (organophosphorylation), its represents an enzymatic inhibition in some cases considered "the target" of toxicity or initial molecular event (IME) in their mode of action developing toxicity (adverse output pathway, AOP). The binding to proteins also represents a sequestration avoiding the OP interaction to other protein. However, there are protein binding OPs (non-catalytic bioscavengers) which can be slowly dephosphorylated, having a role as catalytic scavenger. A proportion of B-esterase activity in serum and brain shows reversible inhibition and their protective role just in situ in the target tissue of toxicity need to be investigated. Serum albumin is other example of B-esterase mainly thorough a tyrosine residue; its role in detoxication have been demonstrated and adducts applied as biomarker of exposure. Moreover, for a specific phosphoramidate family hydrolysis capacity may be enhanced by copper, probably by a mechanism not related with its B-esterase activity. Therefore, we have examples in the borderline between non-catalytic and catalytic scavengers.

Keywords: A esterase; B esterase; scavengers; albumin; phosphorylation