

## MEETING ABSTRACTS

# DEVELOPMENT OF PRE- AND POST-COUNTERMEASURES AGAINST OP TOXINS IN MACAQUES

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Deliberate sarin releases in Syria with large numbers of fatalities emphasize the need for OP countermeasures for both military and civilian populations. Therapeutic countermeasures involve several strategies: (i) preventing OP poisoning through administering pre-exposure treatments that scavenge OPs before they inhibit their physiological AChE targets in the brain and in the periphery (ii) post-exposure oxime that can rapidly reactivate OP-inhibited AChE or (iii) a combination of both. In terms of a pretreatment, our recent studies have demonstrated that administration of an aerosolized (aer)-rHuBChE employing a user friendly nebulizer, forms a protective pulmonary bioshield in the lungs of macaques which to date remains intact for at least 4 days. Thus 8 mg/kg of aer-rHuBChE deposited in the lung can prevent symptoms and inhibition of RBC-AChE and plasma BChE following a high (55ug/kg) inhaled dose of aer-paraoxon (Px) 4 days later; an amount known to inhibit circulating ChEs by >95% and cause tremors. In terms of oxime efficacy, macaque studies have demonstrated that a single IM post-exposure injection of the zwitterionic, centrally acting oxime RS194B (62-80ug/kg) plus low-dose atropine rapidly reactivates OP-inhibited RBC-AChE and circulating BChE and dramatically reverse both early and advanced clinical OP symptoms following lethal inhalation exposure to both sarin vapor (49.6ug/kg) and lethal aerosolized paraoxon (100ug/kg).

The increased efficacy of nebulizers in humans and the known synergy between aer-rHuBChE pretreatment with IM RS194B post exposure bodes well for a prophylactic or combination treatment which can protect against potent inhaled OP agents for >6 days without multiple injections.

*Keywords: aer-human butyrylcholinesterase; sarin; paraoxon; oxime; reactivation; macaques.*

## References

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