

Finding a safe, efficacious and stable vaccine in the ricin protein fold

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Ricin toxin, an extremely potent toxin produced from the bean of the ubiquitous *Ricinus communis* (castor bean plant), has been categorized by the US Centers for Disease Control and Prevention (CDC) as a category B biothreat agent that is moderately easy to disseminate. Ricin has the potential to be used as an agent of biological warfare and bioterrorism. A recombinant ricin toxin subunit A-chain (RTA) antigen was engineered to eliminate the toxin's enzymatic activity and mitigate the undesirable aggregation and precipitation caused by exposure of hydrophobic surfaces on the RTA in the absence of its natural B-chain partner. An Alhydrogel-adjuvanted ricin A-chain 1-33/44-198 vaccine (RVEc™) was manufactured in compliance with cGMPs and evaluated for safety and efficacy during an open-label, uncontrolled Phase 1a escalating, multiple-dose clinical study. Healthy adults (10 per group) received a primary series of 20, 50 or 100 mcg of RVEc™ at 0, 28 and 56 days by IM administration of vaccine. Four subjects in the 50 mcg cohort group consented to a boost with 50 mcg RVEc™ ~20 months from their initial vaccination with subsequent plasmapheresis. Anti-ricin antibodies were purified from plasma and used for correlate of immunity studies in appropriate animal models. The vaccine was safe and well-tolerated at 20 and 50 mcg dose levels. At the 100 mcg dose, 2 subjects had elevated CPK levels after their first vaccination which resolved, but no further vaccinations at that dose were administered. The immune response elicited by the vaccine will be described during the presentation.

Biography

Leonard A Smith received a BA degree in Chemistry and Zoology from the University of New Hampshire in 1972 and his PhD degree in Biochemistry from Georgetown University in 1978. He is the Senior Research Scientist (ST) for Medical Countermeasures Technology at USAMRMC and Scientific Director at USAMRIID. He has authored or co-authored more than 150 scientific publications, reviews and book chapters, and holds several patents for his work on bio-defense vaccine development. He has received numerous awards including the DOD Distinguished Civilian Service Award, the highest award given by the Secretary of Defense to career employees.

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