

Project: Adjuvants that Enhance Natural Resistance Against Mucosal Pathogens

Brief Description: To generate the necessary pre-clinic data on novel countermeasures against select agents of military significance. These compounds enhance natural defense mechanisms of mucosal surfaces of the gut and/or lung.

Executive Summary: Although effective vaccines offer the best long-term solution for protecting military personnel and the public from bio-warfare agents, this approach falls short in several respects. First, development of effective vaccines for many of the organisms on the National Institute of Allergy and Infectious Diseases (NIAID) category A-C list will require considerable long-term research and development efforts for each agent, yet these pathogens pose threats now. Secondly, vaccines under development focus on a single infectious agent, while there are a myriad of threats. Thirdly, some pathogens that may be used in the future may not have been identified, with the result that no vaccines are being developed. Fourth, vaccines do not protect immune-compromised individuals who constitute a growing percentage of the population. Treatments that enhance non-specific resistance to initial colonization by infectious agents (therapeutic and prophylactic adjuvants) offer alternative and complementary approaches to vaccines. Adjuvants can be used against a wide-spectrum of infectious agents, thus time and effort spent on optimizing a formulation for one pathogen extends to multiple diseases. Adjuvants do not have the same problem as anti-microbial drugs with respect to the development of resistance. Furthermore, adjuvant therapy can be used to enhance the natural host defense responses of immune-compromised individuals. New adjuvant materials have been identified that increase resistance to different viral and bacterial infections, including infections by some select agents, and enhance vaccine antigen responses.

Congressional Action Needed: An appropriation of \$2,000,000 is requested.

Importance to the U.S. and Montana: Bio-warfare and bioterrorist acts are a definite reality and represent serious threats to our armed forces and the public. New approaches to counteract these biowarfare agents are needed. This research is designed to identify new classes of drugs that enhance natural host defense mechanisms and thereby, repel a number of infectious agents. MSU has identified a number of novel adjuvants, but needs to expand its preclinical evaluations in preparation to move them through clinical development. It also has the potential to enhance the private sector by new licensing agreements and potential new company spin-offs.

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Adjuvants That Enhance Natural Resistance Against Mucosal Pathogens – Talking Points

- New therapeutic and prophylactic counter measures are needed to combat the increasing bio-warfare threats as specified by the DoD Chem-Bio Defense Program.
- Therapeutic and prophylactic adjuvants offer complementary approaches to vaccines in countering bio-warfare threats. They have activity against a wide-spectrum of pathogens, thus reducing development time.
- High throughput assays were established and used to screen for anti-viral compounds and adjuvants that enhance myeloid cell and epithelial cell functional activity. New lead candidates were identified ahead of schedule and are currently being evaluated in animal models.
- DoD personnel from Chem-Bio visited MSU to expand the partnership.
- New potential “drug candidates” have been identified that: (1) inhibit anthrax toxin, (2) potentially enhance innate resistance to the airborne bacterial agents *Coxiella burnetii*, (3) enhance resistance against multiple pulmonary viral pathogens, and (4) potentially increase epithelial cell resistance to mucosal virus infection and are being tested in animal models.
- With the new containment facilities, MSU is now in position to apply these new technologies toward other DoD priority bacterial pathogens.