



DEFENSE ADVANCED RESEARCH PROJECTS AGENCY
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PM SUMMARY SHEET
SOURCE SELECTION SENSITIVE

Solicitation Number: HR001118S0017
Solicitation Title: PREventing EMerging Pathogenic Threats (PREEMPT)
PM Name: James Gimlett
Proposer: EcoHealth Alliance
Proposal Title: Project DEFUSE: Defusing the Threat of Bat-borne Coronaviruses
Proposal Identifier: HR001118S0017-PREEMPT-FP-019

I have reviewed the attached proposal and Evaluation Reports and find that this proposal is selectable based on the evaluation criteria included in the BAA. However, I am not recommending funding at this time based on the rationale provided below.

Funding Requested (by proposer):

Phase I	Phase II	Total
\$8,411,546	\$5,797,699	\$14,209,245

This proposal aims to identify and model spillover risk of novel, pandemic-potential SARS-related coronaviruses (SARSr-CoVs) in Asia, focusing specifically on known hotspot bat caves in China. In prior work under USAID Predict, the team identified high risk of SARSr-CoVs in specific caves in Asia. The project has a good running start since the hotspot caves already test positive, with high prevalence, for several SARSr viruses so the team won't be looking for needles in haystacks. The team will build on past surveillance work as well as some impressive work in developing geo-based risk maps of zoonotic hotspots based on past spillovers and ecological data. Two approaches are proposed to preempt zoonotic spillover through reduction of viral shedding in the bat caves: 1) innate immune boosting to downregulate viral regulation; 2) targeted immune boosting via vaccine inoculations using chimeric polyvalent recombinant spike proteins to protect against specific high risk viruses.

Two of three reviewers marked this proposal as Selectable. Key strengths are the experienced team and the selected coronavirus hotspot caves that show high prevalence for novel bat coronaviruses. Experimental in vivo and in vitro work is logically thought out and will be used to validate molecular and evolutionary models. Proposed preemption approaches, while somewhat conventional, have the advantage of a fast timeline for validation on bat or "batenized" mouse models. Multiple vaccine delivery mechanisms are proposed, including aerosolized spray, transdermal nanoparticle application, and edible adhesive gels. However, several weaknesses to the proposal were also noted. These include a lack of detail regarding data, statistical analyses and model development and how prior work will be leveraged and extended. Proposal also lacks clear decision points to assess the deployment and validation of TA2 preemption methods in the

wild. Regulatory and ELSI issues are not discussed. Variability of vaccine dose due to variability in delivery mechanisms is also not discussed. In addition, there is concern that vaccine approaches may lack sufficient epitope coverage to effectively protect against the diverse and evolving quasispecies of the many coronaviruses found in the bat caves.

For the above reasons I am not currently recommending funding of this effort. However, there are several components of great interest in this proposed effort that are potentially fundable should additional funding become available.

The team discusses risk mitigation strategies to address potential risks of the research to public health and animal safety but does not mention or assess potential risks of Gain of Function (GoF) research and DURC. Given the team's approach does potentially involve GoF/DURC research (they aim to synthesize spike glycoproteins that may bind to human cell receptors and insert them into SARS-CoV backbones to assess capacity to cause SARS-like disease), if selected for funding an appropriate DURC risk mitigation plan should be incorporated into contracting language that includes a responsible communications plan.

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