

Subject: MTEC Request for Project Information for Systems Biology of Drug-Resistant Infectious Diseases

The Medical Technology Enterprise Consortium (MTEC) is excited to post this announcement for a Request for Project Information (RPI) focused on the use of systems biology approaches to: i) better understand drug-resistant infectious diseases at their molecular, cellular, and systems levels, and ii) identify new potential products and develop them into prototypes for the diagnosis and treatment of these diseases. MTEC's systems biology initiative is focused on utilizing an integrative rather than reductionist approach to understand how biological systems function and interact as a whole. The goal of this initiative is to design an integrated and collaborative research and prototype development portfolio leveraging known or emerging knowledge of the regulatory processes of resistance mechanisms with the purpose of integrated validation, and prototype development with follow-on translation into clinical use. This RPI contains background material and guidance for the preparation of project information paper submissions to the MTEC.

The MTEC mission is to assist the U.S. Army Medical Research and Materiel Command (USAMRMC) by providing cutting-edge technologies and effective materiel life cycle management to transition medical solutions to industry that protect, treat, and optimize Warfighters' health and performance across the full spectrum of military operations. MTEC is a biomedical technology consortium collaborating with multiple government agencies under a 10-year renewable Other Transaction Agreement (OTA), Agreement No. W81XWH-15-9-0001, with the U.S. Army Medical Research Acquisition Activity (USAMRAA). MTEC is currently recruiting a broad and diverse membership that includes representatives from large businesses, small businesses, "non-traditional" government contractors, academic research institutions and not-for-profit organizations.

The MTEC is convening a panel of experts to review the recommendations of USAMRMC's recent State of the Science meeting, Systems Biology of Infectious Disease (details of the State of the Science meeting can be found attached to the full RPI), held for the purpose of identifying relevant pathways of infectious disease resistance in order to better understand those associated with both resistance and its regulatory processes at the molecular level. The panel will develop the research components of a unified plan that identifies known and potentially discoverable processes that regulate bacterial mechanisms of resistance which, as a whole, constitute the likely lion's share of resistance characteristics in bacteria. The research program will emphasize the underlying molecular foundations that sustain these mechanisms of resistance and their associated biomarkers, in order to identify nullifying strategies and countermeasures. The panel's "deliverable" will yield a flexible execution plan that consists of an integrated portfolio of individual activities to be performed by either consortium members or associated academic or other competent collaborators enlisted.

During the meeting, the panel will also identify candidate bacteria to include in the execution plan on such topics as:

- Identify epigenetic biomarkers which may demonstrate or sustain the emergence of resistance, and may be both conserved and/or shared in multiple bacteria, preferably identifying bacteria that may be useful in better understanding the processes and pathways involved in the emergence of resistance;
- Highlight mechanisms underlying resistance in plasmid development, and the mechanisms of plasmid exchange of those which confer resistance to other bacteria;
- Identify microbiome contributions to resistance, and mechanisms that both sustain those molecular exchanges of resistance characteristics, as well as the steps involved in expressing the characteristics of plasmid exchange;
- Identify regulatory mechanisms that contribute to the inactivation of drugs, modification of receptors, and changes in drug metabolism or inhibition and lethal (MIC/MLC) concentration requirements;
- Identify underlying genomic characteristics sustaining the bacteria's ability to regulate and affect gene transfer of resistance;
- Identify mechanisms which underlie/sustain the ability to alter the binding site or effectiveness of antibiotics/antibodies; and
- Other known activities involved in either regulation of resistance mechanisms or associated with the

inherent resistance.

Through this RPI, MTEC is seeking input from both MTEC members and non-members via a project information paper to be considered by the panel. Project information papers will be shared with the panel under non-disclosure agreements. The MTEC may invite one or more of those who submit project information papers to participate in, or present to, the panel during their convening. Please refer to the full RPI for the requirements of the Project Information Paper.

Project information papers are due no later than August 31, 2017 at noon EDT. The RPI will be posted to the MTEC website (www.mtec-sc.org). MTEC membership is NOT required for the submission of a project information paper in response to this MTEC RPI.

Sincerely,

MTEC Project Team

