Abstract Submission for Presenting Research

Scientific Abstract for Consideration

Presentation Theme: Novel health technologies relevant to: military service, with a focus on protection. (CBRNE)

Title of Presentation: Pre-symptomatic screening for identification of diagnostic host-response biomarkers of infection

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Institution or Department: Defence Research Development Canada

Abstract (400 words max.)

Introduction: The first indication of an asymmetric threat event may be when the index case(s) succumb(s) to the threat, thus emphasizing the importance of recognition, diagnosis and treatment. The Innate Immune System is the first line of defence against a variety of challenges, including infection by pathogens, initiating a cascade of signaling events within the body prior to the onset of symptoms. DRDC Suffield Research Centre is probing this early host defence response to determine whether it could be utilized for presumptive identification of an exposure/infection event, since earlier diagnosis can result in earlier treatment initiation, thus potentially improving clinical outcomes.

Methods: Two human surrogate systems, mice and human peripheral blood mononuclear cells (PBMCs), were infected *in vivo* and *in vitro*, respectively, with *B. anthracis* Sterne, *F. tularensis* Live Vaccine Strain and influenza A virus. Samples were collected at various time points early in infection, prior to symptom development, and subjected to microarray, cytokine and agent analyses (culture, PCR). For mouse studies, exposure via the inhalation route was used to mimic the most likely route of infection for humans. Blood samples were analyzed since the long term goal is to develop rapid tests for specific host response biomarkers.

Results: Microarray analysis identified a number of genes that were up-regulated by each agent, in mice and in human PBMCs, indicating mRNAs that have increased transcription rates and/or increased stability following infection. Comparison of microarray results from human and mouse demonstrated that there was some overlap between up-regulated genes in both study systems. Although, *in vitro* PBMC studies do not reflect a system-wide response, they have potential value for narrowing down the selection of genes for futher study in mouse models as they may be reflective of what may happen in humans *in vivo*.

Conclusions: These studies provide knowledge about host responses that could be exploited in the future for determining new assay targets which could indicate early exposure to biological agents, potentially increasing survivability due to an expanded treatment window resulting from earlier diagnosis. The focus of future studies will be on evaluating the identified host-derived disease responsive targets detectable in both animal models and humans, for potential usefulness as diagnostic biomarkers. Sensitivity (simulants) and specificity (other infectious agents) studies will be conducted to determine the usefulness of the biomarkers identified to date, and to determine whether collaboration with industrial partners should be pursued.

Defence Research and Development Canada

External Literature
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