COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

Developing Nanofiber-based Engineered Platforms For Enhanced Armed Forces Health And Biosecurity

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Infectious diseases pose a major non-combat related risk to deployed forces. In addition to the communicable diseases, warfighters may encounter vector-borne diseases, particularly in tropical regions; biological weapons from foreign or terrorist organizations; or novel diseases that emerge in disturbed landscapes. Accordingly, the warfighters need access to both specific and broad-spectrum medical counter measures (MCMs) to prevent and treat a wide spectrum of pathogen threats they could encounter. A sufficiently modular and customizable MCM should counter a variety of example scenarios, such as: A) The pathogen that the troops have been exposed to has been identified, and a fast and effective MCM should be available and stockpiled; B) The personnel are ill with unknown or emerging pathogen, therefore a pathogen agnostic MCM is required; C) Military deployment will be occurring during known epidemic(s) and the personnel need to be vaccinated to boost their immunity, ideally with broad spectrum pan-pathogen vaccines. We will present data on nanofiber-based technologies designed to mitigate each of these scenarios.

Self-assembling peptide nanofibers, a class of biopolymers, are a promising new therapeutic platform, as their structure and function can be controlled through primary sequence design, facilitating multivalent presentation of antigens. One of the well characterized, b-sheet-based, self-assembling peptide nanofiber described in literature is Q11 (QQKFQFQFEQQ), which has been successfully tested as an intranasal reagent to elicit immune response against influenza when conjugated to peptide epitope from viral polymerase. This type of needle free vaccine delivery system is advantageous from a public heath point of view for a multitude of reasons including ease of acceptance, ease of delivery, longer shelf life, and extended temperature stability.

Data from different projects that explore the suitability of Q11 nanofiber technology for the scenarios described above will be presented. Our nanofiber-nanobody chimera for medical countermeasures project explores feasibility of utilizing novel nanobodies to selected pathogens (Influenza virus A, Venezuelan equine encephalitis virus VEEV) and immune cell receptors (CD3 of T-cells) and multivalent display on nanofibers for suitability as MCM to counter scenario A. In our project, DC Recruiter: Pathogen Agnostic Immune Enhancer as Broad Spectrum Anti-microbial we investigate utility of a dendritic cell binding peptide conjugated to nanofiber as a mechanism that could recruit dendritic cells, sentinels of the immune system, to expedite the immune response after an acute exposure (scenario B). We will also discuss the possibilities of developing a nanofiber-based pan-fungal vaccines (scenario C). The methodology and results described will include details of Q11 synthesis, nanofiber assembly and characterization, and conjugation chemistry required to decorate and display peptides and proteins on nanofibers. Methodologies we have developed (e.g. antibody binding, Scanning Electron Microscopy) for verification of functional display of peptides and proteins will be discussed. The modular platform of nanofibers that allows high-density display of multiple components that can enhance both innate and adaptive immune response has the potential to radically improve warfighter health and national biosecurity.
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