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Need for a 'Universal Vaccine' for Select Agents

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Preparedness for bioterrorism or state sponsored warfare using biological agents requires development of effective pre-exposure prophylactic regimen. This is especially important for bacterial agents as post-exposure therapies are plagued with antibiotic resistant strains. Unfortunately, the vaccine development for many of the important select agents is crippled by lack of commercial interest from pharmaceutical/biotech companies. Many state funding agencies, despite their anxiety for the threat perception pertaining to a BTW attack, are reluctant arguably due to, the lack of immediate need (low incidence of bioattack) for these efforts, and their priorities for the agents of public health importance. The US resorted to Strategic National Stockpile (SNS) for an anthrax vaccine and even after decades of efforts, SNS does not have vaccines or drugs to defend against Ebola or plague [1]. Perhaps another reason for this bleak picture of our capabilities to protect against a bioattack is the long list of select agents [2] and an uncertainty of use for a particular agent; as against the endemecity of natural disease outbreaks; it is hard to predict which agent will be used in a bioterror or BW attack. Therefore, a pre-exposure prophylaxis in biothreat scenario warrants immunization with as many vaccines as there are agents or at least agents with potential threat. Even if we have effective vaccines for each of the threat agents, implementing a vaccination programme for this astounding array of causative agents with so many shots is a daunting task even for a disciplined and compliant military population. The only way to handle a civilian population would be based on threat perception and selecting one or two agents for vaccination to a vulnerable group, leaving a question mark on 'preparedness' for biothreat that includes several viral and bacterial agents apart from the toxins and other pathogens.

The vaccine research saw a revolution after the advent of 'reverse vaccinology' [3]; accelerating the rate of discovery of potential vaccine candidates for the pathogenic microbes many fold. The role of traditional vaccinology to eradicate, eliminate, or control a number of infectious diseases cannot be undermined. However, in the biothreat scenario the problems associated with vaccination can be confounded by the number of agents and 'one vaccine-one pathogen' is not a pragmatic solution. Cassonea and Rappuoli [4] highlighted the need for 'fostering the generation of new vaccines that could substantially broaden the spectrum of vaccine-preventable diseases'. We need to work for this highly ambitious 'single vial' that can provide protection for many (if not all) agents of BTW significance. The idea sounds unrealistic and raises several concerns including the immune response to this cocktail, preservation, adjuvant selection, and phase variation of some of the viral and bacterial agents. To identify commonality in the myriad of antigens requires new approaches aided by the high throughput technologies such as pangenomics and proteomics. With the accumulation of whole genome sequence data for multiple strains of pathogens, genomic approaches to identify common antigenic determinants are one way to broaden vaccine coverage at least to a group of infectious agents. Current approaches also include elucidation of 'pathogen-associated molecular patterns' (PAMP) (such as those present in cell surface or cell wall polysaccharides) that are sensed by a host's innate immune system [5]. The other more rationale approach could be augmented by a deeper understanding of host-pathogen interaction. Looking for common pathways that are perturbed by a group of pathogens or universality of host response to a clade of agents can provide valuable clues in this regard. Universality of some of the hitherto unknown effectors from microbes and their targets in the host are valuable themes to start with. It is important to note that several of the subunit vaccines proposed in the recent past, possess enzymatic function and from classical vaccinology view point, sound counterintuitive to provide protection.

Analysis of recent differential proteomic data has indicated that some differential proteins are repeatedly identified, regardless of the experiment and the tissue or species [6,7]. A list of generally detected proteins and proteins families was described by the authors for both human and rodent models. Although shared proteins were identified for neurogenerative and other disease conditions, a similar analysis is lacking for infectious diseases. In another study, Smith and co-workers [8] carried out identification of common biological pathways and drug targets across multiple respiratory viruses based on human host gene expression analysis. Apart from immune response, the up-regulation of host genes, such as protein biosynthetic pathways, play crucial role for pathogen invasion, replication and evasion [9]. Moreover, genetically distinct respiratory viruses often modulate common host proteins and biological pathways during infection [10]. A deeper understanding of host pathogen-interaction, especially under *in vivo* settings, for select agents can provide clues for common pathways and novel targets for developing medical countermeasures against biothreat agents either in the form of 'universal vaccine' or therapeutic measures with expanded spectrum.

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