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

Characterization Of Bacterial Lipid Nanodiscs As Potential Vaccine Candidates

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Proteins are the traditional targets for neutralizing antibodies and vaccines, but evolve rapidly, allowing for escape from immune responses through pathogen variants. Lipids provide promising targets for neutralizing antibodies since they are much less variable among pathogen classes and play key roles in mediating host-pathogen interactions during infection. However, lipids have been associated with poor adaptive antibody responses despite their highly immunostimulatory effects on the innate immune system. This discrepancy may be explained by recent studies showing that presentation of lipids in complex with their host lipid carriers dramatically alters their interaction with the immune system. Nanodiscs comprised of bacterial outer membrane lipids may provide a solution to this discrepancy. Preliminary work done by our lab and others have shown that outer membrane vesicles and nanodiscs can be created from bacterial membrane lipid extracts. However, the lipid content and inter-membrane protein profile as well as their stability under varying conditions including within cells or within the human body have been difficult to characterize. Our work aims to fill these data gaps to rationally design bacterial nanodiscs with defined compositions for future therapeutic and vaccine applications. The goal of this project is to create stable, heterogenous particles from native bacterial lipids without the use of synthetic polymers that can cause adverse reactions artificial nanodisc. These nanodiscs will display an authentic antigenic profile to immune cells and possibly elicit a protective and neutralizing immune response. The protocols to create and characterize bacterial lipid nanodiscs will be applicable to many bacterial pathogens and provide the foundation for a new lipid-based vaccine platform. This novel vaccine platform will allow for quick vaccine product formulation, and possibly eliminate the need for future vaccines and boosters which are based on evolving surface peptides, not the more-constant lipid profile of a pathogen.

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