U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30329-4027

Excellence in Research Work

October 5, 2021

Sun Pharma Science Foundation Research Awards 2021
Sun Pharma Science Foundation
Mumbai, India

Dear Award Committee,

I, Dr. Teena Mohan am herewith offering my candidature for the most encouraging "Sun Pharma Science Foundation Research Awards 2021" in the category of the Medical Sciences— Basic Research. I believe that my strong academic and technical expertise and education make me highly compatible for this esteemed recognition.

I have worked in biomedical sciences, primarily focusing on various infectious diseases in understanding the fundamental principles regulating host's immune functions. Since last more than 6 years, I have worked on various challenging projects based on influenza vaccines, antivirals, pathogenesis, surveillance, and diagnostics in the prestigious organization of United States such as Center for Disease Control and Prevention (CDC), Emory University, and Georgia State University. At this point, I am appealing for this prestigious award— Sun Pharma Research Award— for my GPI- anchored CCL28 chemokine-based research work.

During my tenure with Dr. Richard W. Compans, one of the renowned personalities of the influenza world, in the department of Microbiology & Immunology, Emory University School of Medicine, I worked in evaluating the adjuvant effect of a membrane-anchored chemokine GPI-CCL28 in different projects. These consecutive breakthrough studies were published in recognized scientific journals; Journal of Controlled Release in 2016 and Scientific Reports in 2017.

Chemokines play a vital role in cell migration in response to a chemical gradient by a process known as chemotaxis. CCL28 is a β- or CC chemokine that is involved in host immunity through the interactions with its chemokine receptors; CCR10 and CCR3. CCL28 has been shown to exhibit broad spectrum antimicrobial activity and displays strong homing capabilities for B and T cells and orchestrates the trafficking and functioning of lymphocytes. The CCL28-CCR3/CCR10 circuit is a unifying system that plays a major role in the homing of plasmablasts and plasma cells at mucosal sites. Thus, CCL28 and CCR3/CCR10 receptors perform a critical function in coordinating the inter-dependent innate and adaptive immune responses. As a result, it has become clear that their immunoattractant functions are necessary to translate innate immunity to adaptive immune responses.

In my CCL28 chemokine projects, I studied the adjuvanticity of GPI-anchored CCL28 co-incorporated with influenza HA-antigens in chimeric virus-like particles (cVLPs), in boosting strong protective long-lasting mucosal immune responses through an intranasal route in mice. I compared the immune responses to that from influenza VLPs without CCL28, or physically mixed with soluble CCL28 at systemic and various mucosal compartments.

The VLPs containing GPI-CCL28 showed in-vitro chemotactic activity towards spleen and lung cells expressing CCR3/CCR10 chemokine receptors, and induced antigen-specific antibody titers and avidity indices of IgG in sera and IgA in tracheal, lung, and intestinal secretions that were significantly higher than other vaccine formulations. Significantly higher hemagglutination inhibition and serum neutralization titers against heterologous influenza viruses were also induced by immunization with CCL28-containing VLPs compared to other vaccinated groups. Thus, GPI-anchored CCL28 in influenza VLPs act as a strong immunostimulator at both systemic and mucosal sites, boosting significant cross-protection in animals against heterologous viruses across a large distance.

In another linked study, I examined the long-lasting protective efficacy of cVLPs containing influenza HA and GPI-anchored CCL28 as antigen and mucosal adjuvant, respectively, when immunized intranasally in mice. These cVLPs induced significantly higher and sustainable levels of virus-specific antibody responses, especially IgA levels and hemagglutination inhibition titers, more than 8-month post-vaccination compared to influenza VLPs without CCL28 or influenza VLPs physically mixed with soluble CCL28 in mice. After challenging the vaccinated animals at month 8 with H3N2 viruses, the cVLP group also demonstrated strong recall responses. The results suggested that the GPI-anchored CCL28 induced significantly higher mucosal antibody responses, involved in providing long-term cross-protection against H3N2 influenza virus when compared to other vaccination groups.

This novel vaccine approach may provide exciting new pathways for acquiring broad and effective immunity to pathogens requiring a mucosal site for infection. These revolutionary studies were considered as a promising new method for providing significant breadth of immunity as a candidate universal influenza vaccine. I have continued this novel strategy of GPI-anchored CCL28 chemokine as an adjuvant with tetrameric M2e on self-assembled nanoparticles as candidate universal influenza vaccines. Simultaneously, I have been engaged in studying these GPI-CCL28 chemokine in a dissolvable microneedle patches as a strong immunostimulatory, for the universal influenza painless vaccines approach. I have also been evaluating the role of these cVLPs carrying GPI-CCL28 and influenza HA antigen, in enhancement of T cell immunity and dendritic cells activation and maturation. I have also filled the IP disclosure entitled "Membrane bound CCL28 through GPI-anchoring as an adjuvant" for this novel influenza vaccine approach.

Furthermore, I have been looking forward to work on another β- or CC chemokine; GPI-anchored CCL27 in similar cVLPs, self-assembled nanoparticles, and dissolvable microneedle patches-based studies.

Published Research/Review Articles:

1. Co-delivery of GPI-anchored CCL28 and influenza HA in chimeric virus-like particles induces cross-protective immunity against H3N2 viruses.
   Mohan T, Kim J, Berman Z, Wang S, Compans RW, Wang BZ.
   J Control Release. 2016; 233: 208-19. doi: 10.1016/j.jconrel.2016.05.021. Epub 2016 May 10. PMID: 27178810.

2. Chimeric virus-like particles containing influenza HA antigen and GPI-CCL28 induce long-lasting mucosal immunity against H3N2 viruses.

Mohan T, Berman Z, Luo Y, Wang C, Wang S, Compans RW, Wang BZ.
Sci Rep. 2017 Jan 9;7:40226. doi: 10.1038/srep40226. PMID: 28067290.

3. CCL28 chemokine: An anchoring point bridging innate and adaptive immunity.
Mohan T, Deng L, Wang BZ.
Int Immunopharmacol. 2017 Oct;51:165-170. doi: 10.1016/j.intimp.2017.08.012. Epub 2017 Aug 30. PMID: 28843907.

4. Applications of chemokines as adjuvants for vaccine immunotherapy.
Mohan T, Zhu W, Wang Y, Wang BZ.
Immunobiology. 2018 Jun-Jul;223(6-7):477-485. doi: 10.1016/j.imbio.2017.12.001. Epub 2017 Dec 8. PMID: 29246401.

Total Citation: 77

IP Disclosures Submitted:
1. Membrane bound CCL28 through GPI-anchoring as an adjuvant. Wang BZ, Compans RW, **Mohan T**.

With Best Regards,

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