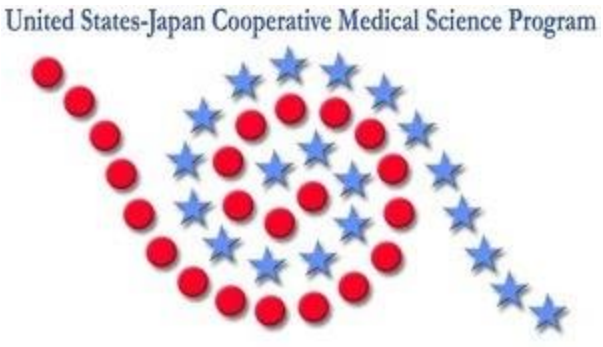

The Joint 24th International Conference on Emerging Infectious Diseases in the Pacific Rim of the U.S.-Japan Cooperative Medical Sciences Program (USJCMSP)

ABSTRACT E-BOOK

March 7 and 8: Immunology Panel

[in order of presentation]

SESSION 1: AI/Data Science-based Prediction of Emerging Infection

Jun Kunisawa - National Institutes of Biomedical Innovation, Health, and Nutrition

Adjuvants for mucosal immunity and Japanese adjuvant and carrier database

Various adjuvants and carriers have been developed to enhance the efficacy of vaccines. The usage of adjuvant or carrier can be determined by the characteristics of the modality used in the vaccine and the immune response required against the target pathogen. With the support of AMED SCARDA program, we have started to establish a database containing information on adjuvants and carriers being developed in Japan. The information in the database includes the not only the immune responses, but also the physical properties, safety, and distribution. In addition, the database has a search function to select appropriate adjuvants and carriers by entering the functions sought by vaccine developers. In this presentation, I will introduce the database, and also present our ongoing research on the development of vaccine adjuvants using components derived from symbiotic bacteria.

Tomoko Hayashi – UCSD

Vaccine Adjuvant Program at University of California San Diego

Vaccines are used to prevent or reduce the severity of infectious diseases and malignancies. However, current vaccines, including subunit or mRNA vaccine platforms, provide only short-term protection, limited efficacy in immune-compromised individuals and are largely ineffective against heterologous strains of pathogens. Thus, adjuvants play a critical role in improving vaccine efficacy to address these limitations. The University of California San Diego has participated in the "NIH Vaccine Adjuvant Program" since 2008 ((https://www.niaid.nih.gov/research/vaccine-adjuvant-research-programs). In this presentation, we describe six small molecule compounds/scaffolds as vaccine adjuvant candidates that promote an innate immune activation, which was discovered under three vaccine adjuvant discovery programs. Two of these compounds, oxoadenine 1V270 and pyrimidoindole 2G053/2G023a, are small molecule ligands for TLR7 and TLR4, respectively. When combined as a TLR7 and TLR4 ligand adjuvant, Fos47, they demonstrated better durability and protection breadth in murine influenza virus challenge models. Fos47 has a high safety profile in mice, and we are currently working on developing it for human influenza or COVID-19 vaccines. In parallel, we have identified four innate immune enhancers under the two recent NIH discovery contracts: 2E151, 2E272, 2F52, and 2H050. 2E151 and 2E272 are calcium-influx-inducing compounds that work as co-adjuvants to the approved TLR4 adjuvant monophosphoryl lipid A (MPL). 2E151 improved antigen-specific antibody production via NFAT activation of innate immune cells. 2E272 increases immune stimulation of extracellular vesicle release from antigen-presenting cells. 2F52 induces aggregation of mitochondrial MAVS protein, and 2H050 inhibits tubulin polymerization, enhancing antigen-specific antibody responses. For these early-stage compounds, we completed preclinical proof of concept efficacy and safety studies and are looking for further opportunities for collaboration that promote research toward the mechanism of action and development of human vaccine adjuvants.

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SESSION 1: AI/Data Science-based Prediction of Emerging Infection

Noriko Sorumachi - University of Tokyo, Japan

Innate Immune Regulation and Lysosome-targeting Drug Development

SESSION 1: AI/Data Science-based Prediction of Emerging Infection

Harry Kleanthous - SK Bioscience, Cambridge, MA / Seoul, South Krea

Vaccine Adjuvant Development

Ken Ishii - Institute of Medical Science, University of Tokyo, Japan

Vaccine Adjuvant Development

Vaccine science was a field that had received little attention prior to the COVID-19, but this changed with the pandemic, and the ripple effect has been far beyond expectations, spreading widely from molecules (academia) to ethics (social contact). The practical application of RNA vaccines is expanding the possibilities of nucleic acid medicine design and science. The practical application of RNA vaccines is expanding the possibilities for the design and science of nucleic acid medicine for the sake of their efficacy as well as safety. It is common knowledge that nucleic acids are genetic information inside the cell, but they are also released outside the cell, where they exhibit specific activities that differ from those inside the cell. In other words, nucleic acids act on immune cells and various other cells as extracellular microparticles, which not only act as adjuvants but also have a wide range of effects on biological phenomena in vivo such as inflammation, cancer, allergy, neurodegeneration, aging, and fibrosis. In this presentation, we will focus on extracellular nano- to micro-particles containing nucleic acids or groups of microparticles that induce the release of nucleic acids to explore the mechanisms of biological responses and their physiological significance and will present the results of our research and development of techniques for measuring and controlling extracellular nucleic acids.

Pi-Hui Liang - ImmunAdd, Taipei City, Taiwan

Sustainable Next Generation Saponin-based Vaccine Adjuvants

QS-21, a purified glycoside from Quillaja Saponaria, is a component of vaccine adjuvant formulated in licensed herpes zoster, RSV, and malaria vaccines. Its widespread use is limited by its structural instability, heterogeneity, and the low yielding of the purification.

ImmunAdd has tackled these issues by developing a Quillaja adjuvant called IA-05. This adjuvant is a truncated analog of QS-21, boasting enhanced purity and stability. IA-05 has demonstrated the ability to improve antigen cross-presentation and extend immune protection. When combined with vaccines targeting SARS-CoV-2, influenza, HBV, and HPV, IA-05 has shown a substantial increase in both humoral and long-lasting cellular immunity compared to approved adjuvants. Notably, no significant body weight changes or hemolysis associated with IA-05 were observed. Importantly, the manufacturing process of IA-05 does not depend on the Quillaja tree, indicating a sustainable supply.

Satoru Nagatoishi - University of Tokyo, Japan

Vaccine Antigen and Antibody Protein Engineering

Our research aims to contribute to developing new therapies for infectious diseases and to developing tools to prevent the spread of infection and infection control by using state-of-the-art engineering techniques. We are further designing and characterizing antibodies using protein engineering to modify antibodies' function with antiviral activity. To develop stable vaccines, we are also evaluating the physicochemical properties of proteins by utilizing the techniques used in biopharmaceutical development. Furthermore, we evaluate the physical properties and functions of proteins and nucleic acids necessary for vaccine development by using multifaceted physicochemical analysis to bridge the gap in designing higher-quality vaccines.

Reiko Shinkura - Laboratory of Immunology and Infection Control

Immunological Evaluation of a Novel Vaccine Adjuvant for Enhancement of Mucosal IgA Antibodies

In the mucosa, IgA antibodies are secreted as multimeric antibodies, which play important roles in normal flora control as well as in infection control. In contrast to IgG antibodies, which are predominantly specific for a single antigen, these mucosal IgA antibodies are known to be broadly antigen-specific, allowing a single type of antibody to respond to multiple antigens.

For SARS-CoV2, it has been shown that multimeric IgM and IgA antibodies can cope with more variants than IgG antibodies. Thus, the development of an effective mucosal vaccine adjuvant that induces mucosal polymeric IgA antibodies provides strong mucosal protection against bacterial and viral infections. This is very different from the conventional vaccine that stimulates the increase of antibody in the serum by intramuscular injection and targets the pathogen after invasion into the body. We believe that it is important for B cells activated by antigens to efficiently migrate to germinal centers in order to induce high-affinity antibodies on mucosal surfaces. We have therefore found a marker for pre-germinal center B cells and are conducting research on substances that induce this marker as novel mucosal vaccine adjuvants. We discuss the evaluation of mucosal immunity of vaccine adjuvants based on intestinal germinal center B cell responses.

SESSION 1: AI/Data Science-based Prediction of Emerging Infection

Yasuhiro Yasutomi - National Institutes of Biomedical Innovation, Health and Nutrition, Osaka, Japan

Non-Human Primate Models for Vaccines