The Role of Sex, Age, and Immunogenetics in Vaccine Response

Biography

Dr Inna OVSYANNIKOVA is the Director of Laboratory-based Studies for Mayo Clinic Vaccine Research Group and a Professor of Medicine at Mayo Clinic. Dr Ovsyannikova brings a comprehensive, systems-level understanding of how sex, age, and race affect innate and adaptive immunity, particularly regarding influenza, measles, mumps, rubella, and smallpox vaccine response. She is a leading researcher in the field of age-related changes and defects in the regulation and function of immune responses to the influenza vaccine virus in elderly persons.

She has published over 240 scientific manuscripts and 17 books/book chapters and has participated in more than 180 scientific exhibits and presentations at national and international societies. Dr Ovsyannikova is the Associate Editor of Vaccine X and also holds current membership in the American Association of Immunologists and the American Society for Microbiology. She has served on many National Institutes of Health (NIH) study sections and international review panels. Dr Ovsyannikova received her Ph.D. degree from the Ilya Mechnikov Research Institute for Vaccines and Sera in Moscow, Russia, and completed her postdoctoral training at the University of Virginia and has two fellowships in Allergy/Immunology and Clinical Pharmacology/Vaccinology at Mayo Clinic.

Dr Ovsyannikova's research areas of interest also include: 1) studies of the genetics of innate and adaptive immune responses to viral and bacterial vaccines, including influenza, measles, mumps, rubella, vaccinia, and anthrax; 2) areas of vaccine-preventable infectious diseases, particularly the application of mass spectrometry/bioinformatics used to develop peptide-

based vaccines against SARS-CoV-2, influenza, smallpox, measles, Zika, and agents of bioterrorism; 3) gene polymorphisms, immunosenescence markers and predictors of vaccine immune response, including adverse events; 4) viral antigen processing and HLA presentation; and 5) systems biology high-dimensional vaccine studies utilizing platforms such as gene expression microarrays, DNA methylation arrays and next generation sequencing (mRNA-Seq, miRNA-Seq, and single-cell mRNA-Seq).

Dr Ovsyannikova's current research is focused on the immune responses to the SARS-CoV-2 virus and the development of a COVID-19 peptide-based vaccine.

Abstract

We investigated whether biological sex, age, and genetic polymorphisms contribute to inter-individual heterogeneity in immunity to several viral vaccines, such as measles-mumps-rubella (MMR), seasonal influenza, and smallpox.

The variability of vaccine-induced immune responses modulated by gene polymorphisms is a significant factor in the protective effect of the vaccination. We previously described genetic polymorphisms in candidate genes, including HLA genes, that are associated with inter-individual variations in antibody responses to several viral vaccines. To expand upon our previous work, we performed genome-wide association studies (GWAS) to discover host genetic variants associated with inter-individual variation in measles, mumps, rubella, and vaccinia vaccine-induced humoral and cellular immune response outcomes. Identifying genetic determinants of the adaptive immune response to vaccine antigens can inform our understanding of vaccine-induced immunity.

Data have shown sex- and age-based differences in adaptive immune responses to many vaccines, leading to variations in protection across populations. Data have demonstrated that

men and women exhibit differences in immune responses to many vaccines, further diminishing equality of protection across populations. Females consistently demonstrate higher antibody responses than males to multiple vaccines, and sex-depended differences in innate and adaptive cellular immune responses have been described. Both hormonal and non-hormonal causal factors have been proposed, but mechanistic relationships remain to be elucidated. Adverse events following vaccination and vaccine effectiveness analyses demonstrated a similar discrepancy. Further, data on sex differences in immune responses to mRNA COVID-19 vaccines are sparse and conflicting. As an example, steeper waning of protective antibody titers post-mRNA COVID-19 vaccination has been associated with male sex.

Age and immunosenescence, and their impact on immune responses after influenza vaccination, are of increasing importance for the development of better vaccines for the elderly. Immunosenescence is an age-related dysregulation of the immune system, which leads to impaired immunity/protection following immunization or infection. This occurs as a result of age-associated changes in innate and adaptive immune system components and is a major contributor to the well-documented increase in morbidity and mortality among older persons after influenza infection and the poorer immune response after vaccination. An enhanced understanding of aging and immunosenescence has profound implications for vaccine use in older populations.

Data from our population-based vaccine studies suggest that vaccine-induced immune responses are significantly influenced by sex, age, and genetic polymorphisms which highlights the importance of these variables in inter-individual variations following vaccination.