

National Institute of Allergy and Infectious Diseases: Effects of Aging and Immune Suppression on the Innate Immune System

This NIH-supported study has shown how the innate immune system may become less effective against infection as people age and stresses the importance of development of new vaccine formulations and other intervention strategies to boost the immune response.

Lead Agency:

National Institute of Allergy and Infectious Diseases (NIAID)/National Institutes of Health (NIH)

Agency Mission:

The mission of the National Institute of Allergy and Infectious Diseases is to conduct and support basic and applied research to better understand, identify, treat, and prevent infectious and immune-related diseases.

Principal Investigator:

Erol Fikrig, M.D.
Department of Internal Medicine
Yale University
300 Cedar Street
Room S525A
New Haven, CT 06520-8031

General Description:

Effects of Aging and Immune Suppression on the Innate Immune System

Understanding the consequences of aging and immune suppression upon infection with, or vaccination against, West Nile virus or influenza is essential to the development of clinical tests and interventions aimed at individuals at particular risk for adverse outcomes in the event of an epidemic. This project focused on the effects of aging and immune suppression on the function of the innate immune system, which is responsible for the body's first response to infection. The NIH-supported project assessed how innate immune system proteins, such as Toll-like receptors (TLRs) and macrophage inhibitory factor (MIF) – two key molecules that direct the innate immune response – may change as people age. Initial findings suggest that the amount and function of different TLRs, such as TLR1, decrease during aging in human innate immune cells. Additionally, when TLR1 and TLR2 are stimulated in older adults, they produce less tumor necrosis factor alpha and interleukin 6, two important proteins that help defend against viral infections. This evidence indicates that lowered expression and function of certain TLRs may be associated with increased infection-related morbidity and mortality and the impaired vaccine responses observed in aging humans. As this project progresses, further studies will assess how these innate immune system mediators change during aging and how

they affect the immune response to infection by West Nile Virus or vaccination against influenza.

Excellence: What makes this project exceptional?

This project assessed the components of the host response that are the first activated by infection; these components represent the initial contact between microbes and host immune cells. This project has identified key parts of the innate immune system that change during aging in humans.

Significance: How is this research relevant to older persons, populations and/or an aging society?

Although it is known that the immune system becomes less effective as it ages, it is not known which specific elements of the immune system break down first. This NIH-supported project will provide an important definition of the changes that occur in host-pathogen interactions in the elderly. Results from this study could have vital implications for vaccine development and immunotherapeutics targeted for the protection of older individuals.

Effectiveness: What is the impact and/or application of this research to older persons?

West Nile Virus and influenza are known to cause greater morbidity and mortality in the elderly than in the general population. The information that is gained from these studies will guide future efforts to develop better diagnostics, vaccines, and immunotherapies for the elderly against these diseases.

Innovativeness: Why is this research exciting or newsworthy?

The innate immune system is critically important in the body's response to many pathogens. In addition to identifying potential mechanisms for augmenting immune responses to West Nile Virus infection and influenza vaccination, findings from this project may also be of general benefit to the treatment and prevention of other types of infections.