AWARD RECIPIENT

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PROJECT
"Influenza Vaccine Immunologic Correlates"

MENTORSHIP TEAM

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Debate about the effectiveness of the influenza vaccine in older adults has been spurred by rising influenza-related deaths despite increasing vaccination rates. Many have recommended that a novel vaccine more immunogenic be developed for a population undergoing immune senescence. A key aspect in developing such vaccines is identifying essential aspects of the aging immune system that recognizes and responds to influenza virus. It is also necessary to find the optimal immunologic correlates to measure vaccine effectiveness in the older population, which is currently unknown. The current standard for evaluating immunogenicity due to influenza vaccination is the measurement of hemagglutination inhibition (HAI). In young healthy adults an HAI titer of 1:40 or greater confers 50% protection against influenza infection. In adults older than 50 years of age, HAI titers tend to be lower than those of young adults and the level of protection provided by an HAI titer of 1:40 or greater is unknown. As opposed to vaccine strategies targeting the humoral immune system, one could postulate that vaccines targeting aspects of the cellular immune system, such as those developed for pneumococcus and varicella, may provide better protection in older adults.

This study will enroll at least 150 subjects per year to assess both humoral and cellular immune responses to influenza vaccines in adults aged 50 years or older and to define which aspects of cellular and humoral immunity correlate with protection from influenza infection.

Objectives:

1. Define which cellular immune responses correlate with protection from influenza infection in adults older than 50 years of age.

Cellular immune response studies will include proliferation assays for both CD4+ and CD8+ T cells, cytokine responses, cytotoxicity assays, and granzyme B measurements. Each of these will be evaluated to see which components of the cellular immune system are protective. Multiple logistic regression models will be implemented to study the relationship between influenza infection and assay responses. Because age, gender and high risk conditions are likely effect modifiers, they will be included in the model and will be evaluated using interaction terms.

2. Determine which humoral immune responses correlate with protection from influenza infection in adults older than 50 years of age.

Analysis will be done to evaluate if a specific HAI titer is indicative of protection from influenza infection. Multiple logistic regression models will be implemented to study the relationship between influenza infection and assay responses. Because age, gender, and high risk conditions are likely effect modifiers, they will be included in the model and will be evaluated using interaction terms.

To date my research has focused on the burden of viral respiratory diseases. Currently, I am evaluating the burden of viral respiratory diseases in older adults and the vaccine efficacy in this group. The support of the ASP-Infectious Diseases Society of America Young Investigator Award in Geriatrics will allow me the opportunity to study the immunologic responses to vaccines in this special group to help explain the results we are finding in the vaccine efficacy studies.