The Effects of Aging on CD4+ T Lymphocytes in Flu Infected Mice

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INTRODUCTION

- Aging is a complex process that reduces immunity and increases susceptibility to and complications of infections in the elderly.
- Ninety percent of influenza-related deaths in the United States occur in older adults.
- The goal of our research is to understand how age-related changes in the immune system impact the course of influenza infection.

OBJECTIVES

- To better understand age-related changes in the immune system and specifically CD4+ T helper cells, we employed a model of CD4+ T helper cell differentiation first described by the Kaech Laboratory using the cell surface markers PSGL1 and Ly6C.
- PSGL1hiLy6Clo are T follicular helper (Tfh)-like
- PSGL1hiLy6Chigh are memory-like
- PSGL1loLy6Clo are Th1 effector
- To further explore the phenotypic changes in Th subsets, we examined gene expression via Real time PCR.

EXPERIMENTAL DESIGN

500 EID₅₀ PR8 Influenza

RESULTS

PSGL1hiLy6Chigh (Tfh) increase and PSGL1loLy6Clo (Teffector) decrease with age in naïve and flu infected populations.

CONCLUSION

- With aging, the Th1 effector subset decreases and the Tfh-like population is increased in both aged naïve and influenza infected mice.
- Comparison of young and aged Th subsets will help determine if changes in gene expression correlate with age-related differences in response to influenza infection.
- We hypothesize that these age-related changes in T helper subset distribution contribute to the declining ability to generate a protective immune response in older individuals.

REFERENCES


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ABSTRACT

Background: To better understand the effects of aging on the immune response in influenza infection, we examined CD4+ Th subsets in aged mice to assess function and phenotype. Influenza-specific Th subsets can be distinguished by expression of cell surface markers PSGL1 and Ly6C. PSGL1hiLy6Clo are memory-like and PSGL1loLy6Chigh are Th1 effectors. To further explore the phenotypic changes in the Th subsets, we examined gene expression via RT-PCR.

Methods: We examined four groups of mice: naïve and influenza infected young (9 wk) and naïve and influenza infected aged (12 mo). Both infected groups were given flu via intranasal infection. Spleens and lymph nodes were pooled from 5 individual mice on Day 0 and post-infection Day 7 for naïve and infected groups, respectively. Fluorescent activated cell sorting (FACS) was performed and gating strategies were used based on PSGL1 and Ly6C protein expression, creating the CD4+ Th cell subsets. RNA was transcribed to cDNA using a reverse transcriptase kit and used in RT-PCR to evaluate gene expression in the Th cell subsets, using preformed PCR arrays.

Results: Th1 effectors (PSGL1hiLy6Chigh) decreased and Th subsets (PSGL1loLy6Cclo) increased with age in naïve and flu infected mice. Gene expression in the infected mice was correlated to Th1 response.

Conclusion: With aging, the Th1 effector subset decreases and the Tfh-like population is increased in both aged naïve and influenza infected mice. Gene expression in the infected mice had more of a propensity for CD4+ Th1 which is involved in defense to viruses. Comparison of young and aged Th subsets will help determine if changes in gene expression correlate with age-related differences in response to influenza infection.