In situ analysis of perforin expression in SIV-specific CD8 T cells in tissues from rhesus macaques vaccinated with live-attenuated SIVΔnef and challenged with SIVmac251

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Introduction

- Human immunodeficiency virus (HIV) was identified as the cause of acquired immunodeficiency syndrome (AIDS) in the 1980s, and since then it has proliferated into one of the most vexing pandemics of its time, if not all of human history. As of today, there is still no known cure for HIV, although numerous strategies are currently being pursued to confer immunity.

- Simian immunodeficiency virus (SIV) infections in rhesus macaques is an excellent model for HIV infection. Currently, the best vaccines to date have been live-attenuated SIV vaccines in rhesus macaques.

- A robust and rapid response by CD8+ T cells has been associated with the immunity provided by live, attenuated SIV vaccines. To characterize this response and identify correlates of protective immunity, I examined the expression of perforin, a cytolytic protein integral to the cytotoxic activity of CD8+ T cells, within virus-specific CD8+ T cells taken from tissues from rhesus macaques.

Methods

- Adult, female Rhesus macaques were immunized with live, virulence-attenuated SIVΔnef and subsequently challenged with pathogenic SIVmac251.

Results

- In genital lymph node tissue from animals sacrificed at varying days before and after challenge, CD8+ T cells that recognize the SIV proteins Tat and Gag were identified in situ using Mamu A*01/Tat tetramers, and perforin was detected using immunofluorescence.

Conclusions

- SIV-specific CD8 T cells are present in the lymph nodes at time of challenge with SIVmac251

- Most of the SIV-specific CD8 T cells were perforin negative, consistent with being central memory cells

- A more complete quantification of levels of perforin post challenge with pathogenic SIVmac251 is underway. These results will provide insights into the phenotype of SIV-specific CD8 T cells associated with protection provided by a live, attenuated vaccine.

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