Abortive influenza specific $CD8^+$ T cell expansion and migration following lethal influenza virus infection.

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Recent studies have demonstrated the important role that $CD8^+$ T cells play in mediating the lysis of influenza infected pulmonary epithelial cells, viral clearance, and protection of the host following influenza virus infections. Therefore, high dose (lethal) intranasal infections have been thought to lead to high virus titers, overwhelming virus replication and lethal injury prior to the development of a protective host $CD8^+$ T cell response. In order to better characterize the evolution of lethal influenza infections, mice were intranasally infected with either lethal or sublethal inoculums of mouse-adapted influenza virus and then analyzed over time for virus titers and antigen load, and the development of influenza virus-specific $CD8^+$ T cell responses. Analysis of pulmonary virus titers and antigen load showed after both lethal or sublethal infections, surprisingly, virus titer/load reached comparable levels within the first 24-48 hours after infection. Furthermore our results show that a pulmonary influenza virus-specific $CD8^+$ T cell response does develop following lethal dose infections, and that the magnitude of the response appears to be inversely related to the initial intranasal inoculum of infectious influenza virus due to an incomplete expansion and migration of $CD8^+$ T cells following lethal infections. Since the development of influenza specific $CD8^+$ T cell immunity is intimately tied to the presentation of viral peptides by dendritic cells to naïve T cells within the pulmonary draining lymph nodes (LN), we examined the migration of respiratory dendritic cells (rDC) from the lungs to the LN following influenza infection and found that rDC appeared to mature and migrate to the LN to a similar extent regardless of the inoculating dose of influenza virus but only did so during the first 24 hours following influenza infection. Therefore the education of rDC within the respiratory tract, prior to their migration to the LN, in response to the initial virus inoculum may be intimately involved in the magnitude of the $CD8^+$ T cell response to influenza virus infection.

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