Possible Escape Mechanisms for SARS Coronavirus Infection

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Her main research interests are in infection and immunity. She works on the developmental biology of antigen presenting cells and T cells, and their roles in bacterial and viral infections. She is also interested in the development of information technology in Medical Education.

Prior to the emergence of severe acute respiratory syndrome (SARS) in 2002-2003, human coronaviruses (CoV) were known to cause relatively mild upper respiratory diseases such as the common cold. The novel SARS-CoV, however, caused severe, rapidly progressive atypical pneumonia with fever, myalgia and diarrhoea. The detection of virus in stool and urine in addition to the respiratory tract of SARS patients further suggested that SARS is a systemic disease.

At autopsy, white pulp atrophy was observed in the spleen and there was lymphoid depletion in lymph nodes. Together with lymphopenia and increasing viral load in the first 10 days of disease, these clinical features strongly suggest an evasion of the immune system by SARS-CoV. As with other viral infections, such as measles, this lymphoid depletion may have pathogenic significance.

Dendritic cells (DCs) are antigen presenting cells which play key roles in linking innate and adaptive immunity. Immature DCs reside in the respiratory tract for immune surveillance and they respond dynamically to local tissue inflammation in the airways and the distal lung. They express a wide range of receptors, including c-type lectins and toll-like receptors, for the recognition of conserved pathogen patterns. Dendritic cells signal the presence of danger to cells of the adaptive immune response and modulate their responses via the secretion of proinflammatory and/or antiviral cytokines.

The migration of DCs from tissues to lymph nodes is essential for antigen presentation and triggering of adaptive immune responses. The trafficking of DCs is regulated by chemokines which can be classified as homeostatic (constitutively expressed) or inflammatory (induced/augmented) according to their immune functions. Acute respiratory viruses commonly induce inflammatory chemokines, such as macrophage inflammatory protein (MIP)-1α, regulated upon activation, normal T cell expressed and secreted (RANTES), interferon-inducible protein of 10kD (IP-10) and monocyte chemotactic protein (MCP)-1, in local tissues. Dendritic cells are also a major source of these chemokines.

Based on the function of DCs in immune surveillance, priming and tolerance, we hypothesized that DCs play an important role in the immunopathology of SARS. In addition, the developmental status of the host immune cells may affect their responses to viral infection. Hence, we compared the cytokine and chemokine gene expression in SARS-CoV infected adult and cord blood DCs. Our study provides evidence that SARS-CoV can infect DCs and alter their cytokines/chemokines production. The lack of antiviral cytokine response against a background of intense chemokine upregulation could represent a mechanism of immune evasion by SARS-CoV.

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