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Severity of Infectious Mononucleosis (IM) Correlates with the Frequency of Crossreactive Influenza A Virus (IAV)-M1 and Epstein Barr Virus (EBV)-BMLF-1-specific CD8 T Cells

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Et al.

Severity of infectious mononucleosis (IM) correlates with the frequency of crossreactive influenza A virus (IAV)-M1 and Epstein Barr virus (EBV)-BMLF-1-specific CD8 T cells

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During EBV-associated IM IAV-specific crossreactive memory T cells are activated and play a role in disease severity. In HLA-A2+ IM patients, influenza $M1_{58}$ (IAV-M1)-specific CD8 memory T cell responses crossreacted with two different EBV lytic epitopes, $BMLF1_{280}$ (17/29) and $BRLF1_{190}$ (19/20). Furthermore, 11/22 IM patients demonstrated some intra-viral crossreactivity between EBV-BRLF1 and -BMLF1 responses. Disease severity of IM directly correlated with significantly increased frequencies of crossreactive IAV-M1/EBV-BMLF1, IAV-M1, and EBV-BMLF1 specific CD8 cells, and with mean viral load over the first 5 weeks of infection. Disease severity did not correlate with BRLF1 or M1/BRLF1 crossreactive responses. When severity of IM was scored and patients were assigned to either mild or severe groups, disease severity correlated with specific TCR Vb usage in IAV-M1 population suggesting that TcR selection is driving disease outcome. Consistent with IAV-M1 and EBV-BMLF1 responses driving increased immunopathology was the observation that patients with severe disease had significantly more IAV-M1 and EBV-BMLF1 cells producing IFNg/MIP1-b in response to antigen as compared to patients with mild disease. These results suggest that T cell crossreactivity impacts T cell selection and function and ultimately disease outcome. Insights on these issues are important for the intelligent design of vaccines and to develop therapeutic interventions for virally induced disease (NIHAI49320).