May 20th, 12:30 PM

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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Aslan, Nuray; Watkin, Levi B.; Gil, Anna; Luzuriaga, Katherine; and Selin, Liisa K., "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" (2014). *UMass Center for Clinical and Translational Science Research Retreat*. 8.  
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Comments
Abstract of poster presented at the 2014 UMass Center for Clinical and Translational Science Research Retreat, held on May 20, 2014 at the University of Massachusetts Medical School, Worcester, Mass.

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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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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\textsubscript{58} (IAV-M1)-specific CD8 memory T cell responses crossreacted with two different EBV lytic epitopes, BMLF1\textsubscript{280} (17/29) and BRLF1\textsubscript{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).