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Rabinarayan Mishra
University of Massachusetts Medical School

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Crossreactive Epstein-Barr virus (EBV)-Influenza A virus (IAV) specific CD8 memory T cells during acute symptomatic IAV infection.

Rabinarayan Mishra¹, Anna Gil¹, Nuray Aslan¹, Katherine Luzuriaga², Liisa K. Selin¹

¹Department of Pathology, ²Department of Molecular Medicine, University of Massachusetts Medical School, Worcester

We previously showed that crossreactivity is common between IAV and EBV in HLA-A2+ patients during infectious mononucleosis. IAV-M1-GIL₅₈₋₆₆ specific CD8 T cells, along with expanded populations of IAV-M1-GIL₅₈₋₆₆/EBV-BRLF1₁₀₉₋₁₁₇-YVL and IAV-M1-GIL₅₈₋₆₆/EBV-BMLF1₂₈₀₋₂₈₈-GLC double-tetramer+ cells were detected directly ex-vivo in 5 HLA-A2+ patients. Altered IAV-M1₅₈₋₆₆, EBV-BRLF1₁₁₉₋₁₁₇ and -BMLF1₂₈₀₋₂₈₈ TCR repertoires were observed over the course of infection and in comparison to healthy donors. After culture, cells were sorted and analyzed by gene array in order to assess global changes in immune responses following different stimulations, either cognate or crossreactive, in different patient populations. M1-GIL and BRLF1-YVL specific cells had similar immune-response gene signatures, but the -GLC specific CD8 cells were more similar to the two-crossreactive populations. Crossreactive M1-GIL/BRLF1-YVL cells from the BRLF1-YVL line were different in their activation status than the BRLF1-specific cells, consistent with BRLF1-YVL ligand stimulation of different gene activation profiles in these two populations. These results suggest that during symptomatic IAV infection there is an expansion of EBV/IAV crossreactive memory CD8 T cell responses. Ongoing studies are investigating whether EBV-IAV cross-reactive CD8+ T cells may contribute to immunopathology during acute IAV infection (NIH / NIAID PO1 AI 049320).

Contact: Rabinarayan.Mishra@umassmed.edu

Ph-508-856-6314