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Acute Symptomatic Influenza A Virus (IAV) Infection in Humans Leads to Expansion of Highly Diverse CD8 T Cell Repertoires Crossreactive with Persistent Epstein Barr Virus (EBV)

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Et al.

Acute symptomatic Influenza A virus (IAV) infection in humans leads to expansion of highly diverse CD8 T cell repertoires crossreactive with persistent Epstein Barr virus (EBV)

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The competence of T cell responses predominantly depends on how efficient T cell receptors (TCRs) are at recognizing antigenic epitopes. We show here that during acute severely symptomatic IAV infection there was an expansion of IAV-M1/EBV-BRLF1 and IAV-M1/EBV-BMLF1 double-tetramer+ cells directly ex-vivo in 5 HLA-A2+ patients. We questioned whether this expansion specific to these two different crossreactive responses would lead to alterations in the TCR repertoire of the IAV-$M1_{58}$, EBV-$BRLF1_{109}$ and -$BMLF1_{280}$ from before, during and following acute IAV infection. Using staining with Vb MAb we found that T cell responses generated to these epitopes became surprisingly more polyclonal, with the sharing of Vb between M1, BMLF1 and BRLF1 populations which is not seen in healthy donors and which decreased 2 months later consistent with crossreactive expansion. Furthermore, by using single-cell analysis of TCRα and TCRβ repertoire of tetramer sorted IAV-M1 cells we showed dramatic changes in specific clonotype usage and in JA and JB family usage during acute IAV infection compared to before infection. In summary, these changes in TCR repertoire during acute symptomatic IAV infection suggest that during severe infection there is a preferential expansion of highly diverse crossreactive responses between IAV and the persistent virus, EBV, which leads to permanent changes in TCR repertoires to both of these two viruses. (NIHAI49320).