



Figure S3: Functionally crossreactive CD8 T-cells in middle-aged EBV-SN adults lyse EBV-infected and peptide-coated autologous BLCL targets. **a.**) Representative examples of increased lysis of EBV-infected targets by IAV-M1-specific cells in all 3 shortterm cultures from Donor 1 (i)& 2(ii). In  $^{51}\text{Cr}$ -release assays, CD8 $^{+}$  T-cells from indicated cultures were used as effectors and incubated with targets for 5 hrs at 37 $^{\circ}\text{C}$  at indicated effector:target ratios to measure cytotoxicity. Targets used were either autologous WT or BZLF1 KO BLCLs stimulated with PMA to induce EBV lytic cycle. This lack of BZLF1 protein expression results in the inability of the cells to enter lytic cycle and express lytic crossreactive antigens BMLF1 and BRLF1. **b.**) Lytic unit (LU) representation of increased specific lysis of EBV-infected targets in (a). One LU is defined as the number of effector cells required to lyse 15% of  $5 \times 10^3$  target cells during the 5-hour assay. **c.**) Increased lysis of cognate IAV-M1, and crossreactive BMLF1 and BRLF, vs control peptide-coated autologous BZLF1 KO BLCL targets by IAV-M1 cultures of donor 1 and 2. **d.**) Lytic unit (LU) representation of increased specific lysis of peptide-coated targets as seen in (c) for all 3 cultures of both donors.