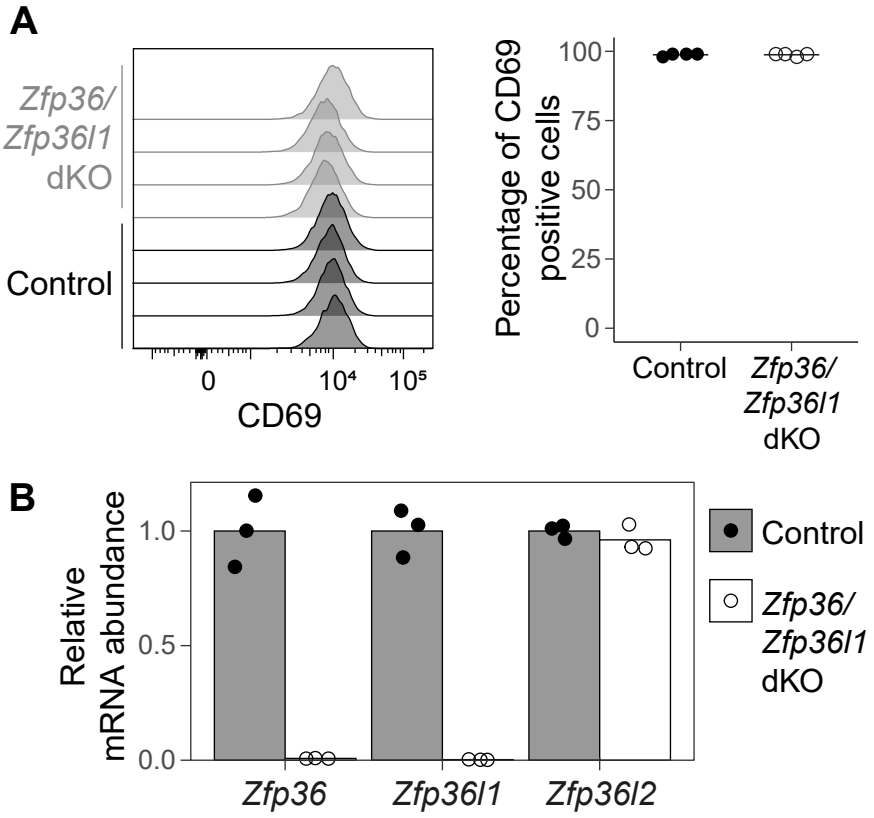

Figure S1. Efficient CD4-cre-mediated deletion of *Zfp36* and *Zfp36l1* does not affect cell activation (**A**) Flow cytometric quantitation of CD69 expression by control and *Zfp36/Zfp36l1* dKO CD4⁺ T cells following 24h activation with anti-CD3 and anti-CD28. (**B**) Abundance of mRNA for Zfp36-family genes, measured by quantitative RT-PCR before and after activation of control and *Zfp36/Zfp36l1* dKO CD4⁺ T cells with anti-CD3 and anti-CD28. For each gene, abundance is quantified relative to the mean abundance for control samples prior to activation.

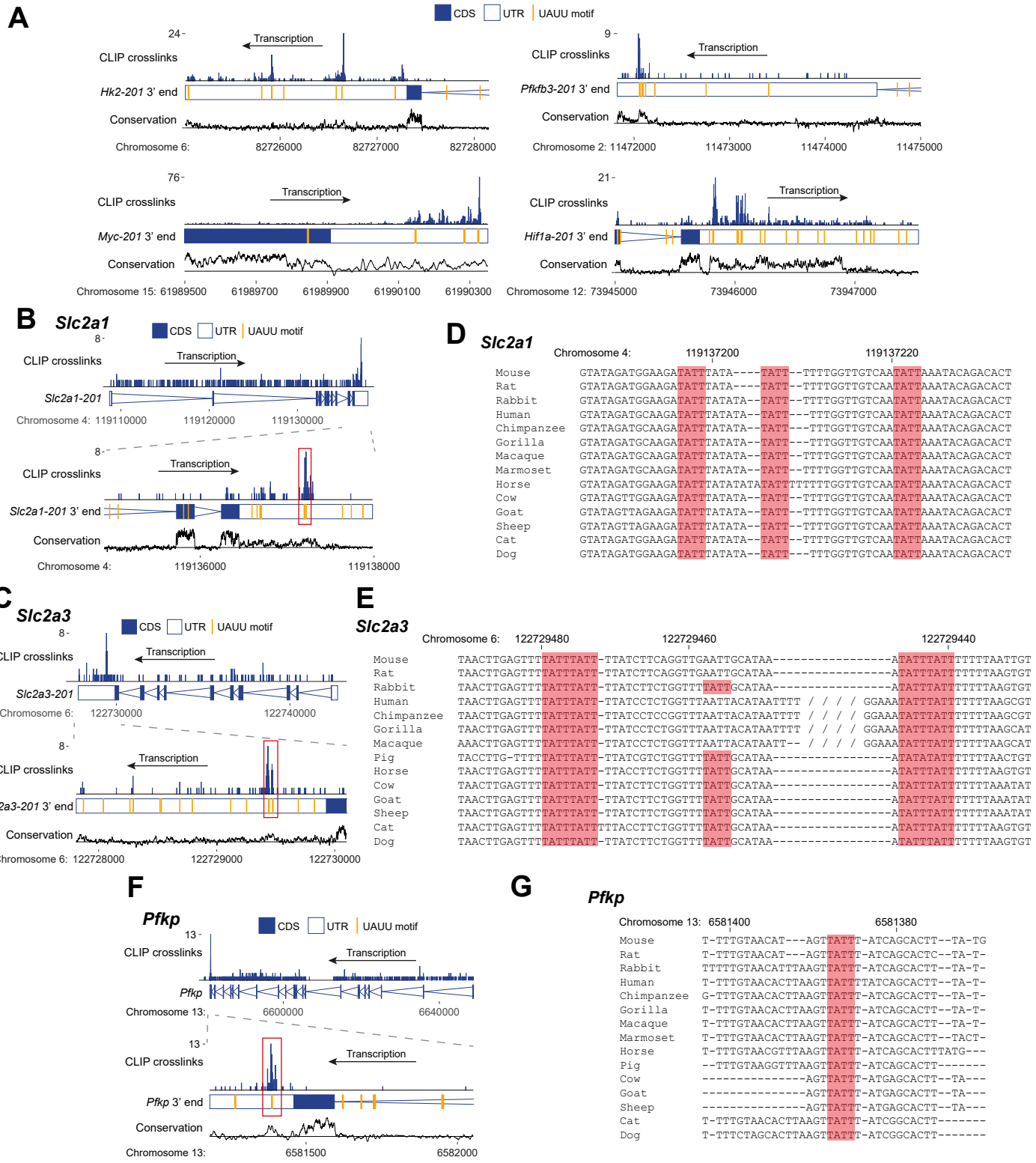

Figure S2. Direct targeting by ZFP36-family RBPs of genes encoding glycolytic enzymes. (**A**) ZFP36/ZFP36L1 crosslinks in the 72h HITS-CLIP data over the 3'UTRs of the indicated transcripts. Occurrences of the UAUU motif are shown as vertical orange lines. Conservation tracks represent phyloP scores from a 60-way multiple alignment, averaged over a sliding 7 bp window. (**B-G**) ZFP36/ZFP36L1 crosslinks in the 72h HITS-CLIP data and multiple sequence alignments of the regions indicated by red boxes over the indicated *Slc2a1* (**B**, **D**), *Slc2a3* (**C**, **E**) and *Pfkp* (**F-G**) transcripts. For **B**, **C** and **F**, top panel depicts the whole transcript; bottom panel is zoomed in on the 3'UTR and depicted as described for **A**. In **D**, **E** and **G**, TATT (UAUU) motifs are highlighted, and genomic coordinates for the mouse 3'UTR are indicated.

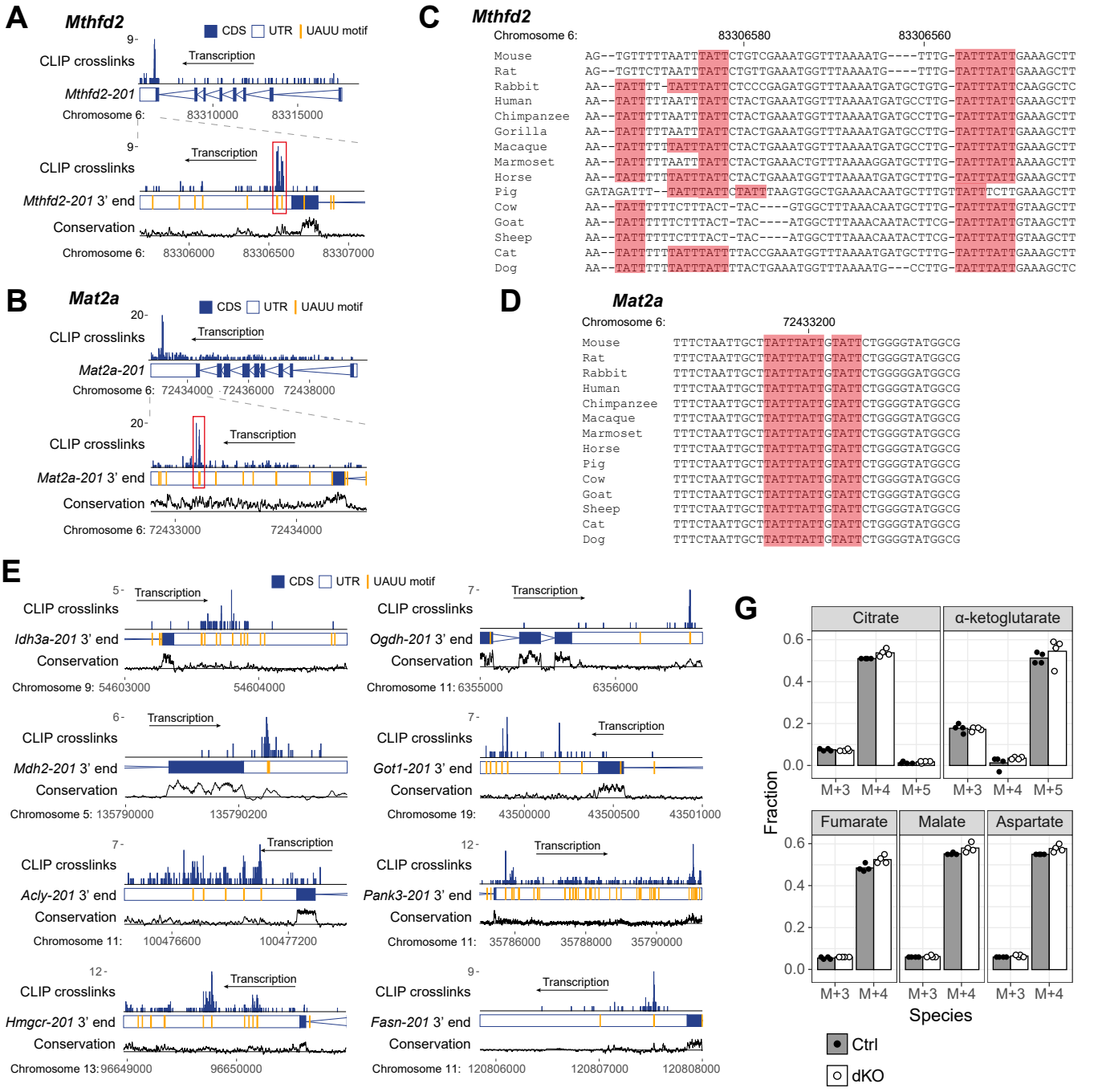

Figure S3. Regulation of metabolic genes by ZFP36-family RBPs (**A-D**) ZFP36/ZFP36L1 crosslinks in the 72h HITS-CLIP data and multiple sequence alignments of the regions indicated by red boxes over the indicated *Mthfd2* (**A**, **C**) and *Mat2a* (**B**, **D**) transcripts. For **A** and **B**, top panel depicts the whole transcript; bottom panel is zoomed in on the 3'UTR and additionally shows occurrences of the UAUU motif as vertical orange lines. Conservation tracks represent phyloP scores from a 60-way multiple alignment, averaged over a sliding 7 bp window. In **C** and **D**, TATT (UAUU) motifs are highlighted, and genomic coordinates for the mouse 3'UTR are indicated. (**E**) ZFP36/ZFP36L1 crosslinks in the 72h HITS-CLIP data over the 3'UTRs of the indicated transcripts, depicted as described for the bottom panel

of **A** and **B**. (**F**) Relative abundance of the indicated metabolites in dKO compared with control $CD4^+$ T cells following 24 hours activation, meausred by LC-MS. (**G**) Fractional abundance of TCA cycle metabolites that had incorporated 3 (M+3 species), 4 (M+4) or 5 (M+5) labelled carbons following 24 hours activation of control and dKO $CD4^+$ T cells in the presence of ^{13}C-labelled glutamine.

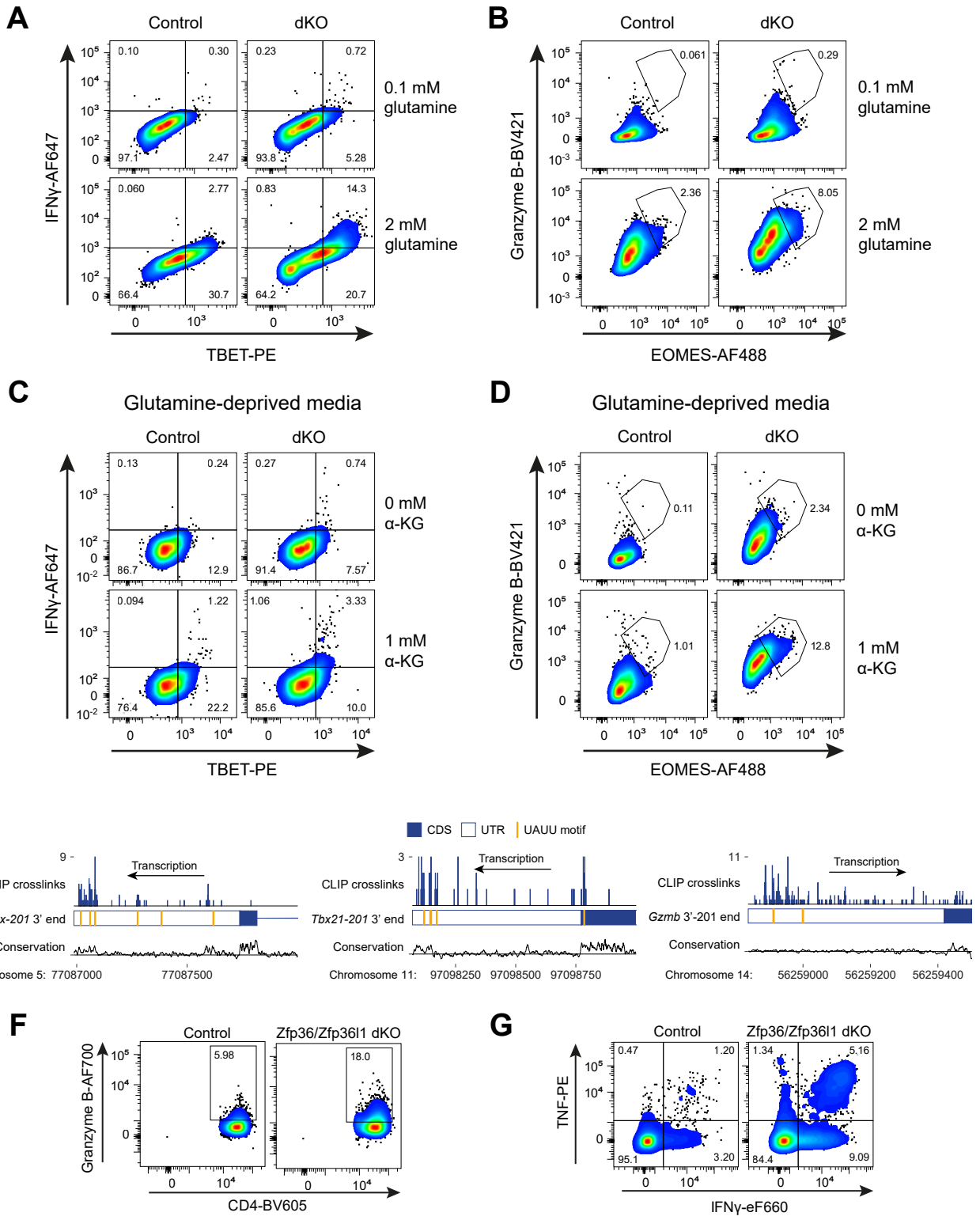

Figure S4. ZFP36 and ZFP36L1 impact CD4⁺ T cell differentiation. (**A-D**) Representative flow cytometry plots for one control and one dKO sample, showing TBET and IFNγ (**A**, **C**) or EOMES and Granzyme B (**B**, **D**) expression by CD4⁺ T cells following activation with anti-CD3 and anti-CD28 in Th1-polarising conditions for 24 hours, followed by a further 48 hours maintenance in IL-2, with varying concentrations of glutamine (**A**-**B**) or esterified α-ketoglutarate (**C**-**D**). In each case, representative plots for the maximum and minimum concentrations are shown. (**E**) ZFP36/ZFP36L1 crosslinks in the 72h HITS-CLIP data over the 3'UTRs of the indicated transcripts. Occurrences of the UAUU motif are shown as vertical orange lines. Conservation tracks represent phyloP scores from a 60-way multiple alignment, averaged over a sliding 7 bp window. (**F**-**G**) Representative flow cytometry plots for one control and one dKO sample, showing EOMES and Granzyme B (**F**) or TNF and IFNγ (**G**) expression by CD4⁺ T cells isolated from the lung 10 days following infection with influenza A virus.