1. We record the log2FC data corresponding to Supplementary Fig 9a and the CD8+multimer+ % of T cells data corresponding to Supplementary Fig 9b in the paper [www.nature.com/articles/nbt.4303](http://www.nature.com/articles/nbt.4303) (same source as 1 Hamming mutational scan, Fig. 1e). The raw data is not available, neither are the heatmaps in vector graphics format. So we save the heatmaps as webp files, convert to jpg files, read pixel-wise RGB values using a Python code and then map the RGB values to log2FC values using the colorbar.
2. Just as the 1 Hamming logFC, we clipped negative values of the logFC to 0. To assign TCR activation categories, we note, by comparing Figs. 1d,e (source of 1 Hamming data) and 1i (where >1 Hamming log2FC range matches recorded data from Fig. S9a), that the plotted 1 Hamming log2FC values are not identical in these two cases, denoting some kind of normalization difference across them. For >1 Hamming data, thus, we used the maximum of 1 Hamming log2FC from Fig. 1i (=5.2, estimated from the yscale in Fig 1i) to normalize 2-Hamming data, and correspondingly assigned TCR activation categories according to the normalized values.
3. For flow % data, <=% for the irrelevant peptide (0.03%) is considered NB, >0.03% but >=1.25% (which is half of index peptide %) is considered WB and >=1.25% is considered SB.