

## **TCR affinity rules T cell activation: a threshold exists**

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Specific binding of T cell receptor (TCR) to antigenic peptide/MHC (pMHC) complexes initiates T cell activation and thus adaptive immune response. Whether TCR affinity or ligand off-rate determines the fate of T cells in vivo has long been argued and is still unclear, although both have some supporting evidence from earlier studies. We have analyzed the interactions between P14 TCR and 56 altered gp33 peptides (LCMV) in complex with mouse class I MHC D<sup>b</sup>. We found 21 peptides bound to D<sup>b</sup> efficiently by pMHC stability assay. We then screened these peptides for differences in their ability to stimulate cytotoxic CD8<sup>+</sup> T cells in vitro by chromium release assay. Using surface plasmon resonance (SPR), we directly measured the affinity (Kd) and kinetics ( $k_{off}$ ) of interactions between P14 TCR and these peptide ligands. Whereas all peptides showed similar off-rates at seconds' level, TCR affinity seemed to dominate in TCR cytotoxic response. Binding of pMHC of higher affinity led to higher cytotoxic lysis. Interestingly, several peptides that induced high CTL responses (IC50 at nanomolar level) showed similar affinity for P14 TCR, indicating the existence of a threshold. Different avidity of peptides of same affinity could come from other factors such as coreceptor binding. Our results argue for an affinity threshold model.

## **Background and aims**

## **Methods**

Surface plasmon resonance was used to directly measure the affinity and kinetics of the interactions between peptide-MHC and P14 TCR.

## **Results**

Fig 1 pMHC stability assay

Fig 2 SPR data

Fig 3 CTL data

Fig 4 CTL vs. SPR

## **Summary**

## **Reference**

Malherbe L, Hausl Christina, Teyton L, and McHeyzer-Willams MG. *Immunity*, 21: 669-679