

Figure 1

Alignment of the TCR ζ -chain. A) An alignment of the full ζ -chain across multiple species reveals a high degree of conservation of all three ITAMs. B) An alignment of the three ζ -chain ITAMs in humans reveals that with the exception of the defining features of the ITAM motif itself, there is very little sequence homology between the three ITAMs. Given the conservation across species, this suggests a functional role for differences between ζ -chain ITAMs within a species.

doi:10.1371/journal.pcbi.1003004.s001

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Figure 2

Ultrasensitivity in the absence of ZAP-70 can be mediated by differential affinities of Lck, CD45, or both. A) The total phosphorylation of TCR ζ -chain is shown as a function of the concentration of active Lck to CD45 in the absence of ZAP-70. When both Lck and CD45 have identical ITAM affinities or put another way, when there are no differential affinities, we observe a small Hill number (none, orange curve). Ultrasensitivity is improved if Lck, CD45, or both have differential ITAM affinities (red, green, blue curves, respectively). As for ZAP-70, the differential affinity is achieved by keeping the on-rate identical but varying the off-rate by 10-fold between each ITAM. The catalytic rate is identical between each ITAM. B) Hill numbers for each case in panel A. Note that the increased ultrasensitivity relies on the Lck affinity to increase from membrane-distal to membrane-proximal ITAM while the CD45 affinity must increase from membrane-proximal to membrane-distal, which we have assumed to be the case.

doi:10.1371/journal.pcbi.1003004.s002

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Figure 3

An alternate measure of sensitivity for the heat map in Fig. 5B. We repeat the calculations in Fig. 5B except display the ratio of EC to EC on a log-scale (i.e. $\log(EC/EC)$) instead of the Hill numbers. We find identical trends and can therefore conclude that the Hill number is a reasonable measure of sensitivity.

doi:10.1371/journal.pcbi.1003004.s003

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Text S1

BioNetGen source code used to generate the wild-type systems model of T cell receptor proximal signaling.

doi:10.1371/journal.pcbi.1003004.s004

(PDF)