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Clonal Selection of Helper T Cells is Determined by An Affinity Threshold With No Further Skewing of TCR Binding Properties

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Helper T cell responses that focus the TCR repertoire of responding clones provide experimental access to the mechanisms of clonal selection in vivo. Using TCR β chain animals, we directly evaluate the extent of TCR α CDR3 diversity and the pMHCII binding attributes of individual antigen-specific Th cells. Here, we demonstrate that dominant clonotypes, as defined by TCR junctional sequence similarities, are surprisingly diverse at the level of pMHCII binding properties, before and after antigen exposure. During an immune response, we can detect and quantify the selective loss of antigen-specific clonotypes that express lower affinity TCR. This affinity-threshold selection is followed by the unbiased propagation of preferred clonotypes regardless of TCR-pMHCII half-lives or affinity. We propose that this unique selection mechanism serves to establish and maintain functional heterogeneity among antigen-experienced Th cells in vivo.