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Abstract

T cells bearing αβ T cell receptors (TCRs) recognize antigen as peptides bound to class I or class II major histocompatibility proteins (MHC). TCRs on mature T cells are usually very specific, for both peptide and MHC class, isotype and allele. They are picked out from a precursor population in the thymus by MHC-driven positive and negative selection. Here we show that the pool of T cells initially positively selected in the thymus contains many T cells that are very cross reactive for peptide and MHC and that subsequent negative selection primarily establishes the MHC-restriction and peptide specificity of peripheral T cells. Our results also suggest germ line encoded TCR variable elements have an inherent predisposition to react with features shared by all MHC proteins.