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The molecular basis of TCR germline bias for MHC is surprisingly simple

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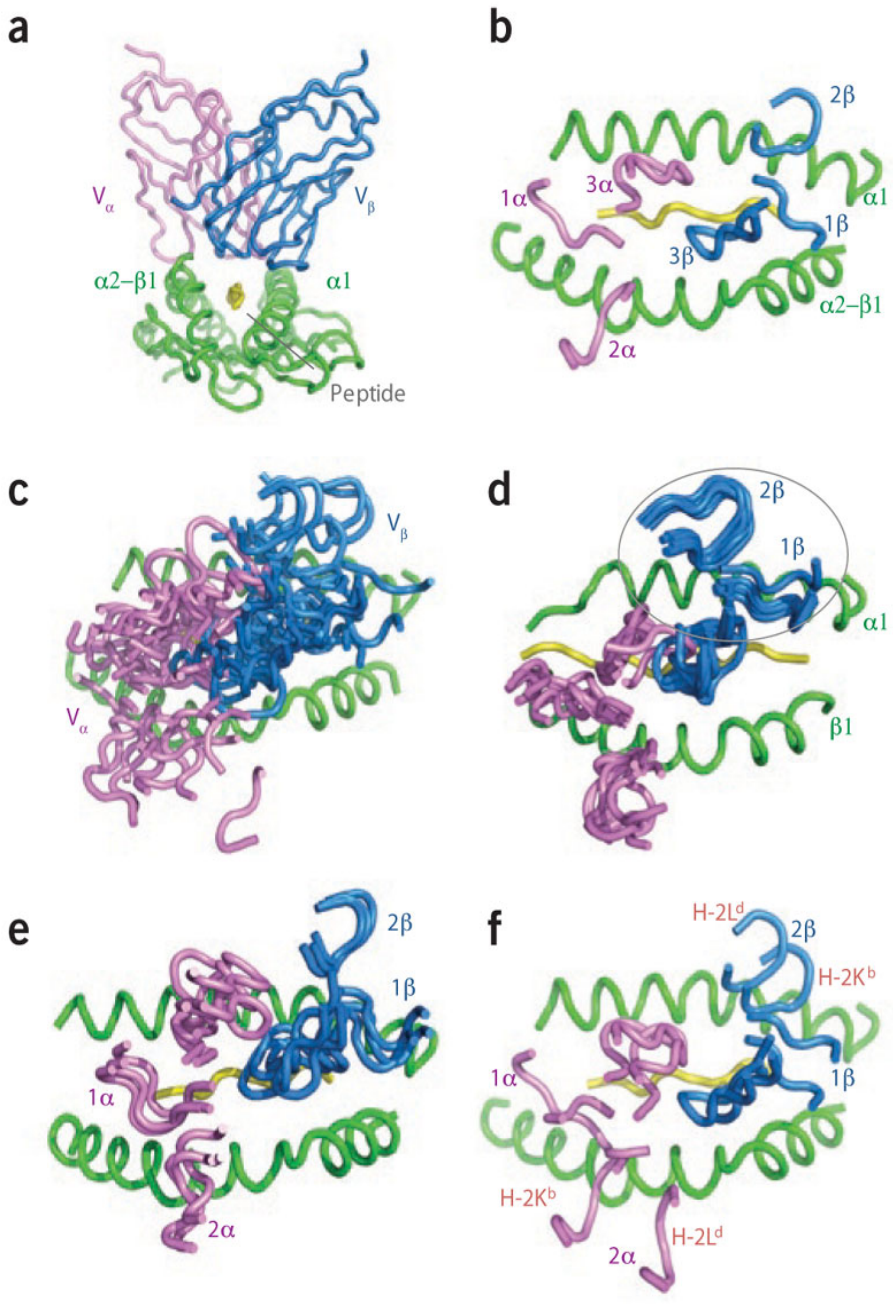

(**a**) Interaction of $V_\alpha V^\beta$ with peptide-MHC, viewed down the MHC groove (Protein Data Bank accession number, 2CKB). (**b**) 'Footprint' view of **a** showing the stereotyped polarity of the V_α and V^β CDR loops on pMHC. (**c**) Convergent footprint polarity but diverse CDR loop positions in nine different TCR-pMHC complexes (Protein Data Bank accession numbers, 1AO7, 1FO0, 1J8H, 1KJ2, 1ZG1, 2NX5, 1MI5, 1OGA and 1U3H). (**d**) Close superpositions (in circle) of the contacts of $V^\beta 8$ CDR1 and CDR2 with the I-A MHC α1 helix in six different TCR-pMHC complexes (Protein Data Bank accession numbers, 1U3H, 2Z31, 2PXY, 1D9K, 3C60 and 3C61). (**e**) Retention of similar germline-mediated contacts by the BM3.3 TCR with H-$2K^b$ in three different peptide complexes (Protein Data Bank accession numbers, 1FO0, 2OL3 and 1NAM). (**f**) Use of alternative 'codons' for interaction of the 2C TCR V_α and V^β with H-$2K^b$ versus H-$2L^d$ (Protein Data Bank accession numbers, 2CKB and 2OI9). H-$2K^b$ and H-$2L^d$ (in red) adjacent to the respective loops indicate the positions of CDR2α and CDR2$^\beta$ in the structures.