Sequence of the TCR β chain gene used by a T cell clone specific for the synthetic polymer, GAT

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The murine immune response to GAT, a synthetic polymer of glutamic acid⁶⁰:alanine³⁰:tyrosine¹⁰, is of particular interest for two reasons. First, the ability to generate an immune response to GAT is under genetic control (1). Second, the immunoglobulin (Ig) molecules produced by GAT-specific B cells are unusually homogeneous (2); a single VH gene segment (3, 4) and at most 2 V κ gene segments (5) encode most of the anti-GAT Ig. Given the unique aspects of this immune response, it is possible to determine whether GAT-specific T cells are as homogeneous as GAT-specific B cells and whether the T cell receptors (TCR) used in recognizing GAT share regions of sequence similarity with the anti-GAT Ig.

The gene encoding the β chain of the TCR was identified as a rearranged J β -containing DNA fragment that was unique to BB02' (3), a GAT-specific helper T (Th) cell clone. This fragment was cloned into λ gtWesB; the internal fragments containing the V, D, and J gene segments were then subcloned into M13 and sequenced. As presented below, the rearranged TCR β chain gene from BB02' contained in-frame joins of the V β 4 (6), D β 2, and J β 2.3 (7) gene segments and there was no evidence of somatic mutation. To ascertain that this was in fact the expressed gene, replicate slot blots containing BB02' RNA were hybridized with seven V β probes; only V β 4 hybridized.

The protein sequence predicted from this V β gene was then compared with the V κ and VH polypeptides used by GAT-specific B cells. Interestingly, there were no regions of significantly greater similarity between these sequences than between any random β and Ig polypeptides. This was true even when comparing the critical V(D)J junction regions. Lastly, to determine whether other GAT-specific T cells utilize the same TCR, a series of 17 V β probes was hybridized in parallel to slot

blots containing RNA from another Th clone, BD01' (3), and from a series of 22 GAT-specific T-cell hybridomas (Zborowski and Kraig, unpublished). Of these 23 additional T cells, only one contained detectable levels of V β 4 RNA. This suggests that the GAT-specific TCR repertoire is more heterogeneous than the anti-GAT B cell repertoire.

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      1      G P V D P K I I Q K P K Y L V A V T G S E K I L
      CCACAG GT CCA GTC GAC CCG AAA ATT ATC CAG AAA CCA AAA TAT CTG GTG GCA GTC ACA GGG AGC GAA AAA ATC CTG
      Leader      V $\beta$ 4 gene segment
      78      I C E Q Y L G H N A M Y W Y R Q S A K K P L E F M F
      ATA TGC GAA CAG TAT CTA GGC CAC AAT GCT ATG TAT TGG TAT AGA CAA AGT GCT AAG AAG CCT CTA GAG TTC ATG TTT
      156      S Y S Y Q K L M D N Q T A S S R F Q P Q S S K K N H
      TCC TAC AGC TAT CAA AAA CTT ATG GAC AAT CAG ACT GCC TCA AGT GCG TTC CAA CCT CAA AGT TCA AAG AAA AAC CAT
      234      L D L Q I T A L K P D D S A T Y F C A S S Q E R G S
      TTA GAC CTT CAG ATC ACA GCT CTA AAG CCT GAT GAC TCG GCC ACA TAC TTC TGT GCC AGC AGC CAA GAG AGG GGT TCT
      D $\beta$  gene segment
      312      S A E T L Y F G S G T R L T V L
      AGT GCA GAA ACG CTG TAT TTT GGC TCA GGA ACC AGA CTG ACT GTT CTC GGTA
      J $\beta$ 2.3 gene segment      Intron

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