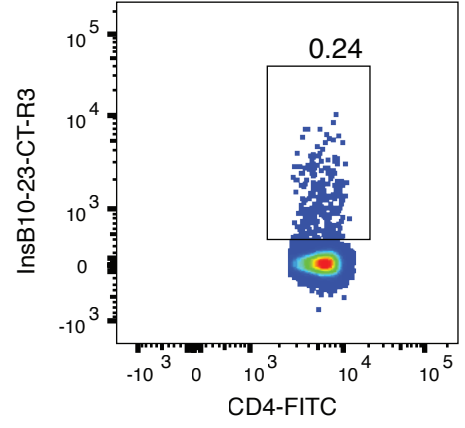
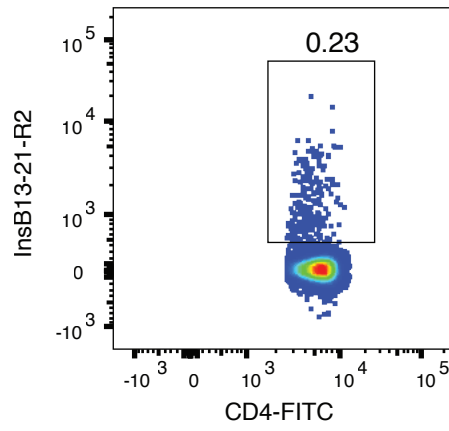
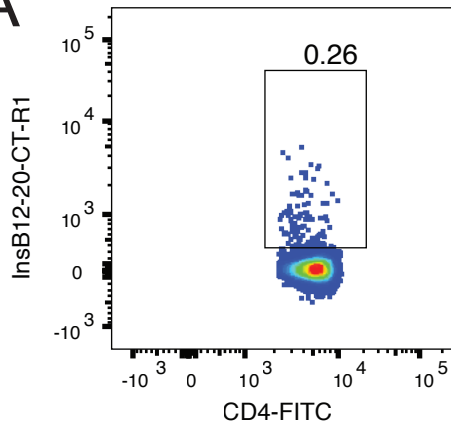
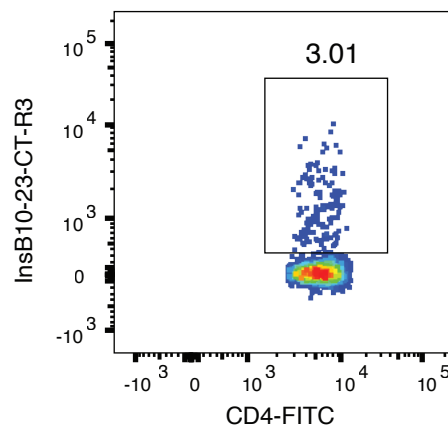
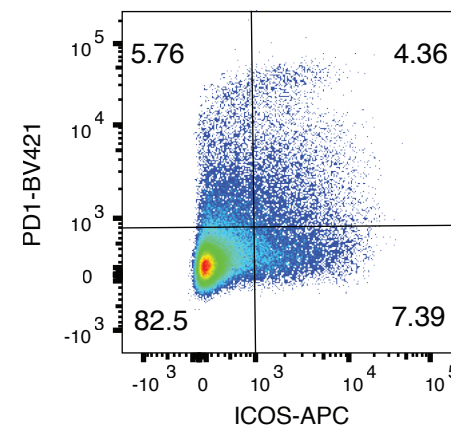
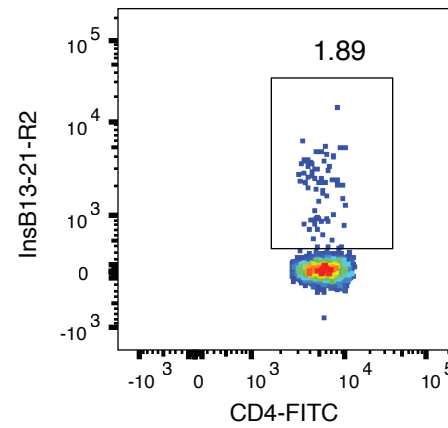
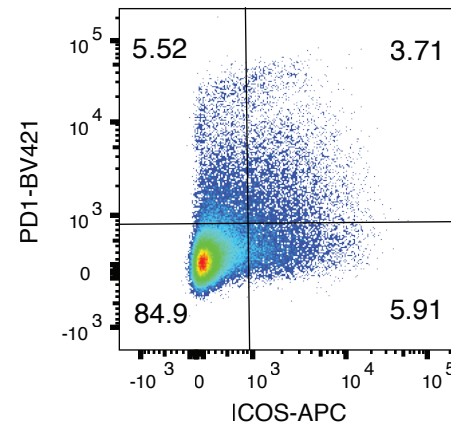
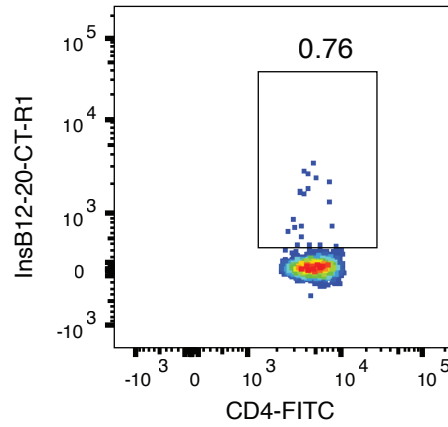
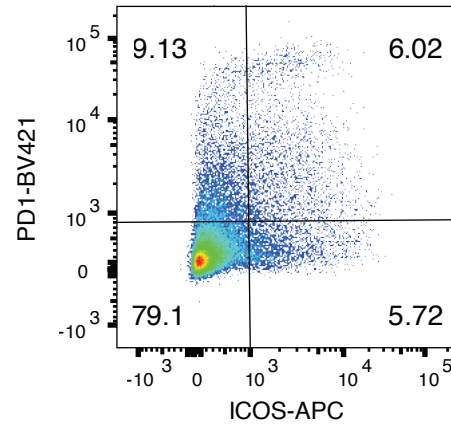


A

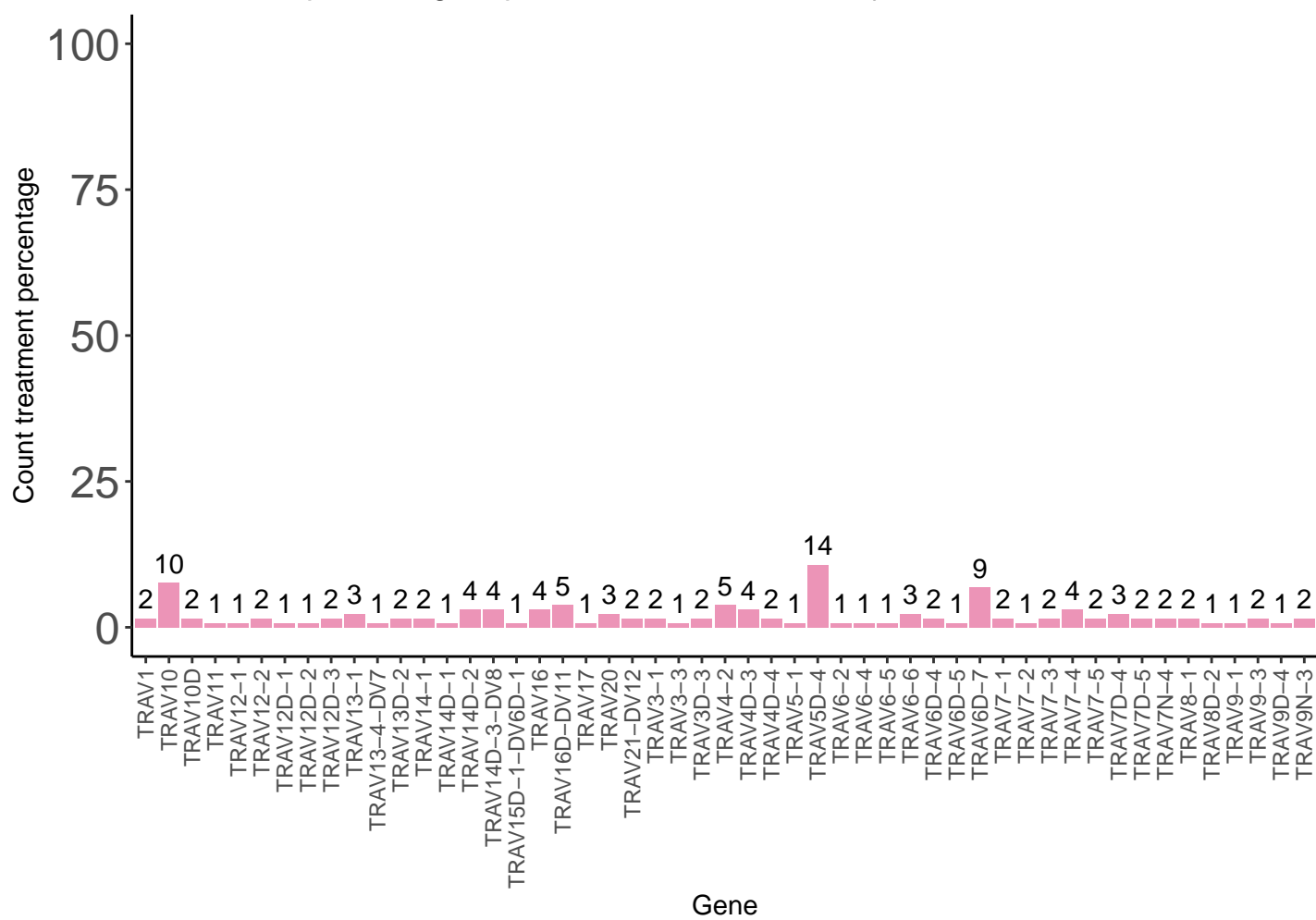


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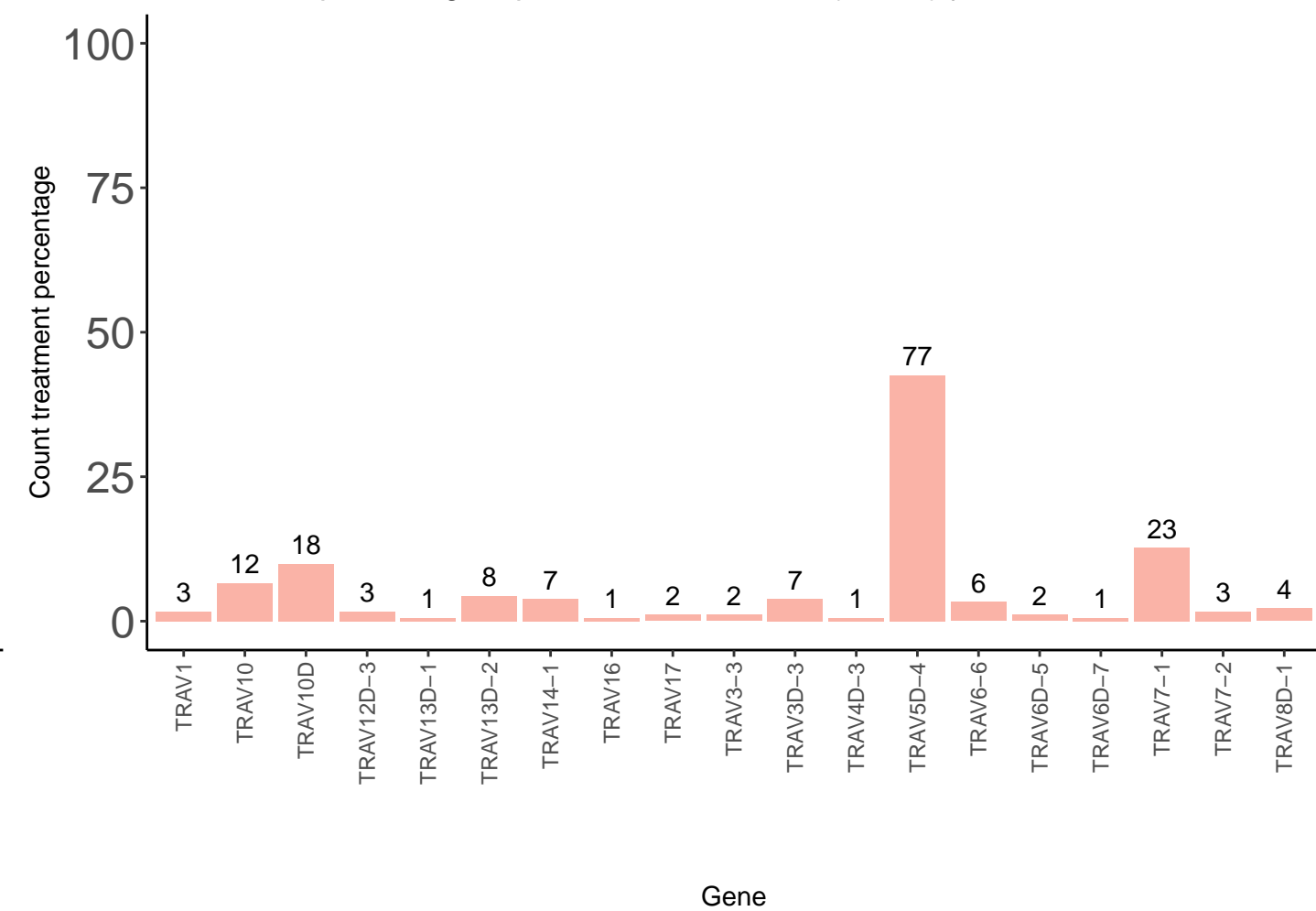


**Supplementary Figure 1. A**, pMHCII tetramer/CD4-FITC staining profiles for pooled splenocytes from pMHCII-NP-treated mice (n=5 mice/group). Profiles correspond to CD4+B220<sup>-</sup> cells. **B**, Gating strategy for sorting Tetramer<sup>+</sup> TR1-like CD4<sup>+</sup> T-cells for scRNAseq studies. Left, ICOS (APC) and PD-1 (BV421) staining within the splenic CD4+B220<sup>-</sup> T-cell pool. Right, pMHCII tetramer staining within the ICOS<sup>+</sup>/PD-1<sup>+</sup> gate (Q2 in middle plot). Tet<sup>+</sup>/ICOS<sup>+</sup>/PD-1<sup>+</sup> cells were sorted for transcriptomic studies.

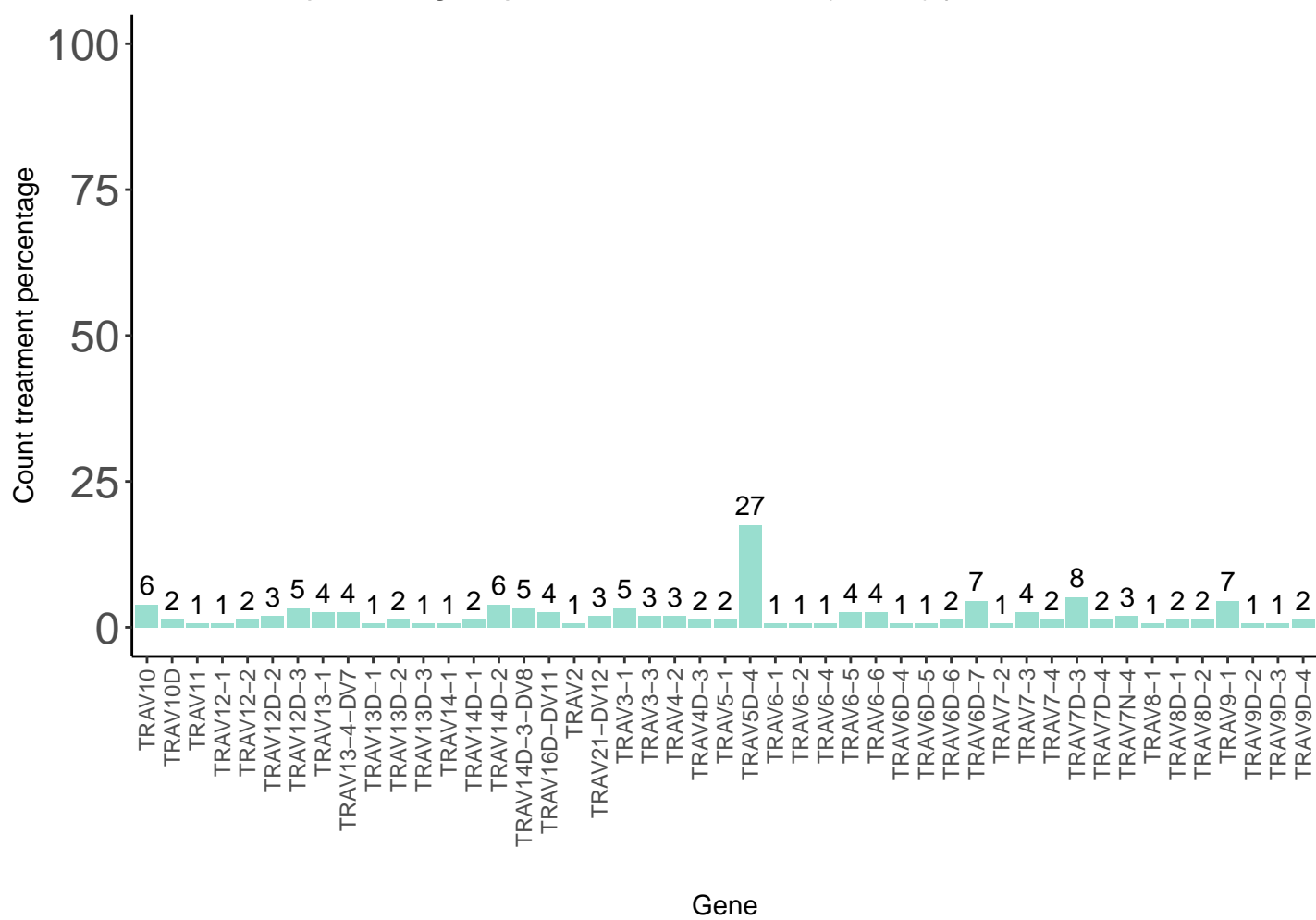
Gene count percentage Alpha Genes: Control\_Tet- | Total: 131



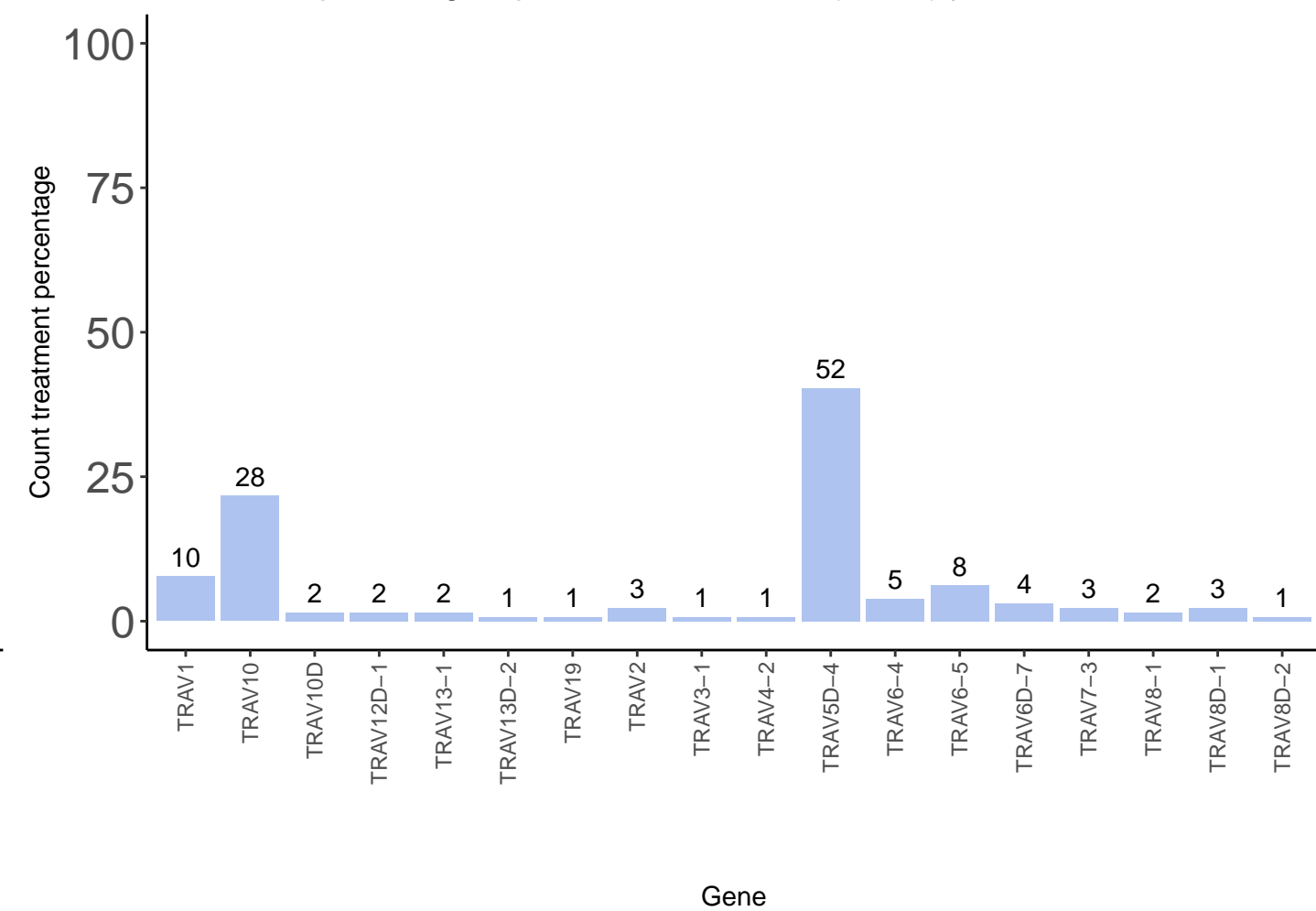
Gene count percentage Alpha Genes: Tet+\_InsB(10-23) | Total: 181



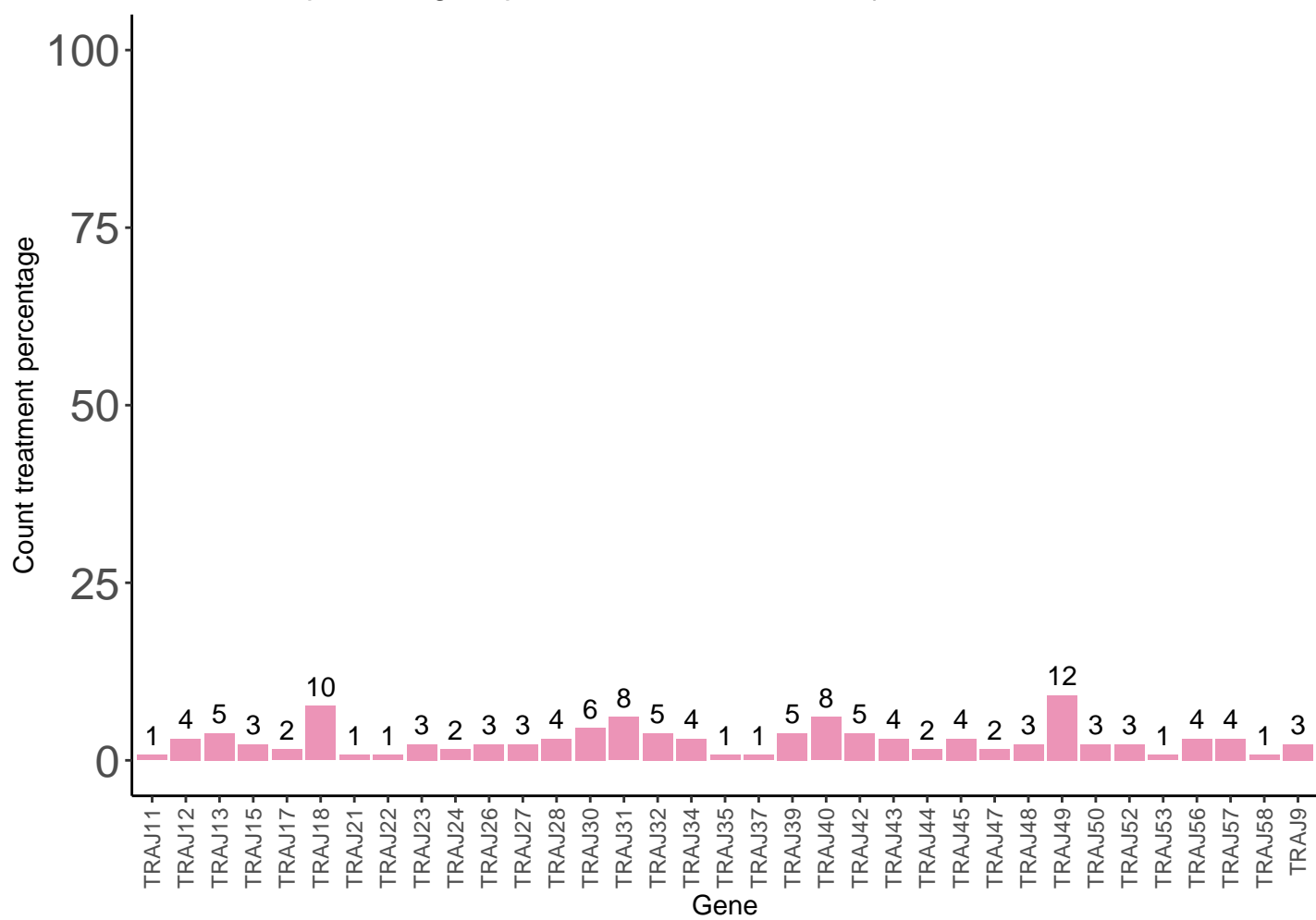
Gene count percentage Alpha Genes: Tet+\_InsB(12-20) | Total: 154



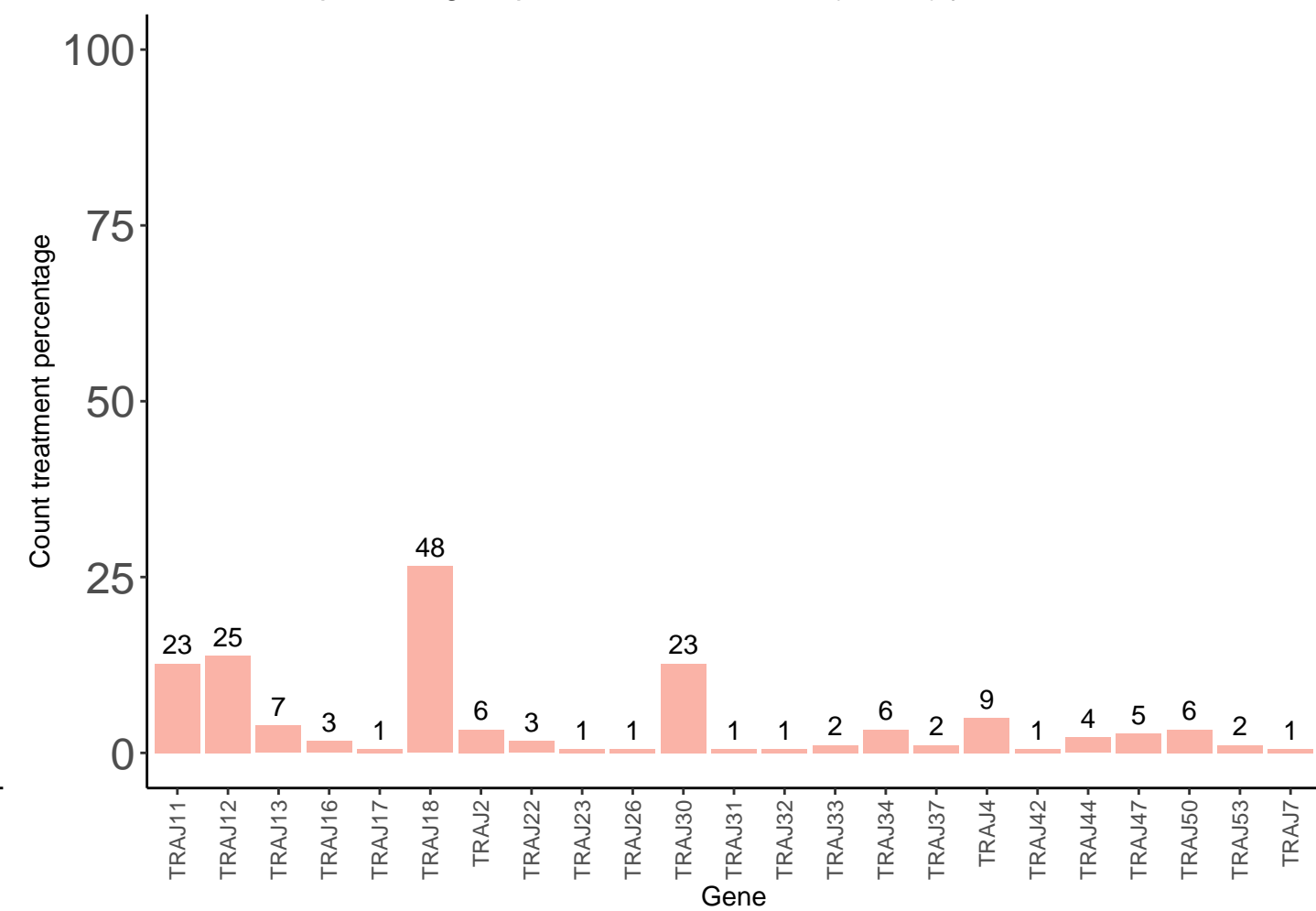
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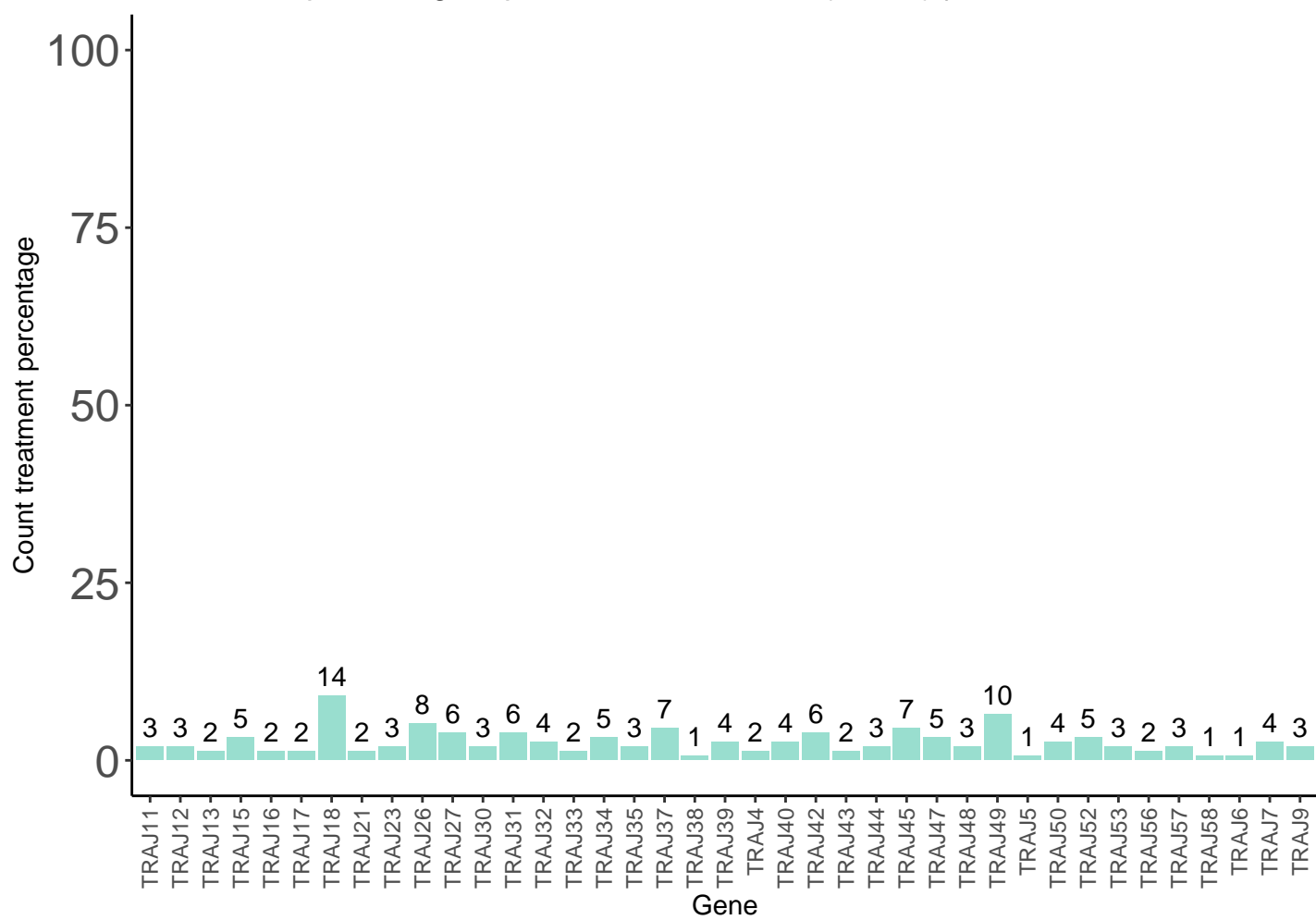
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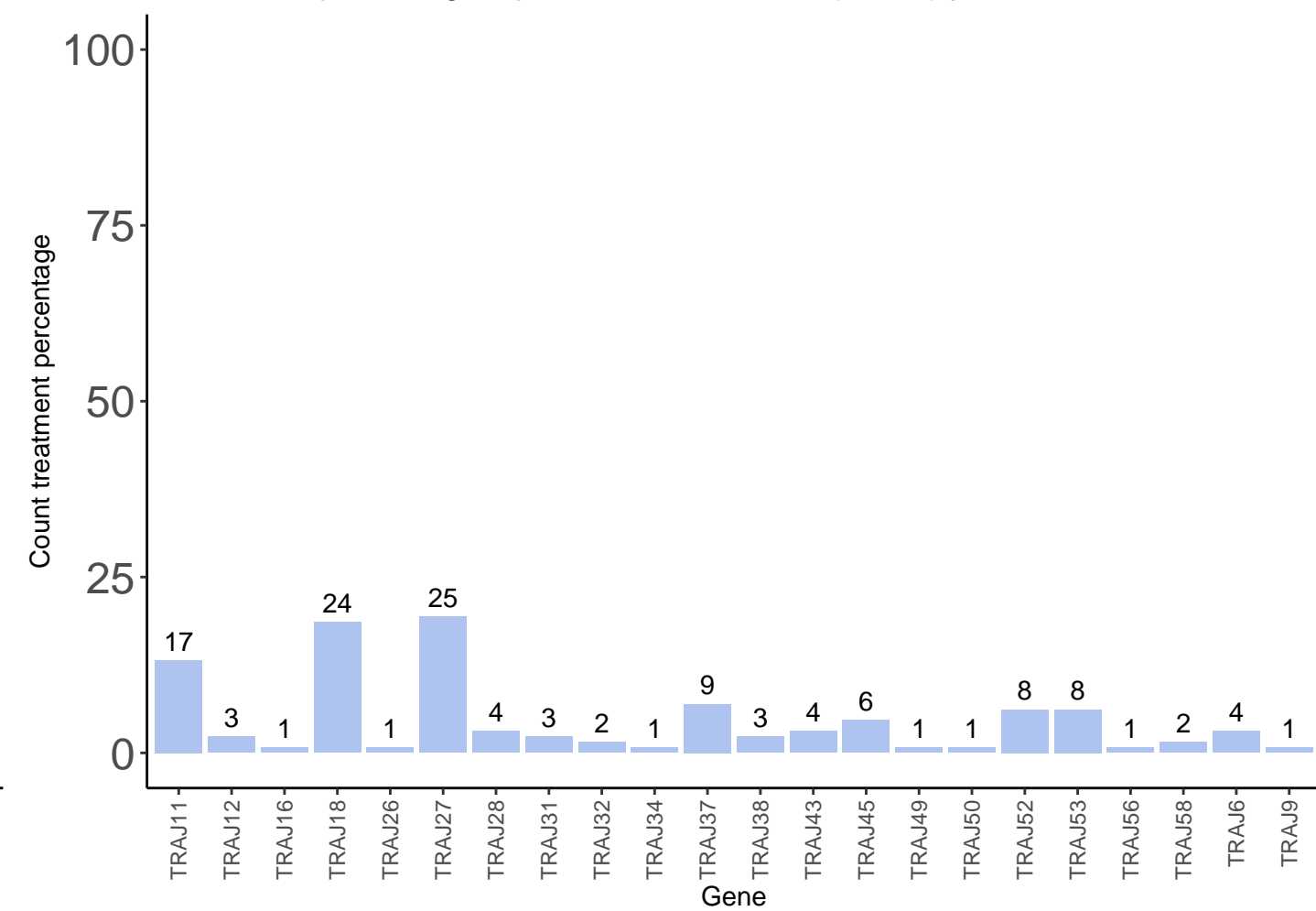
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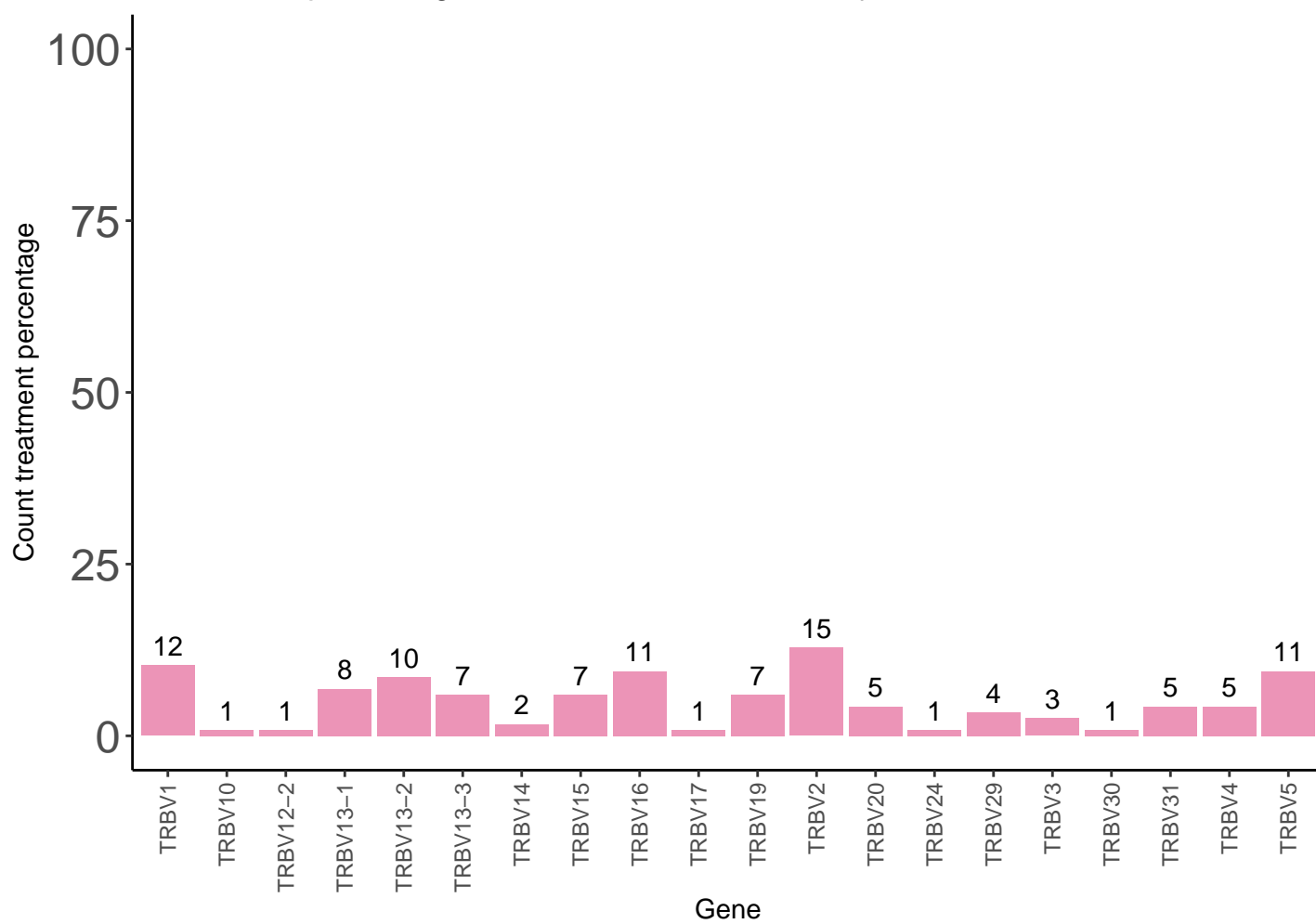
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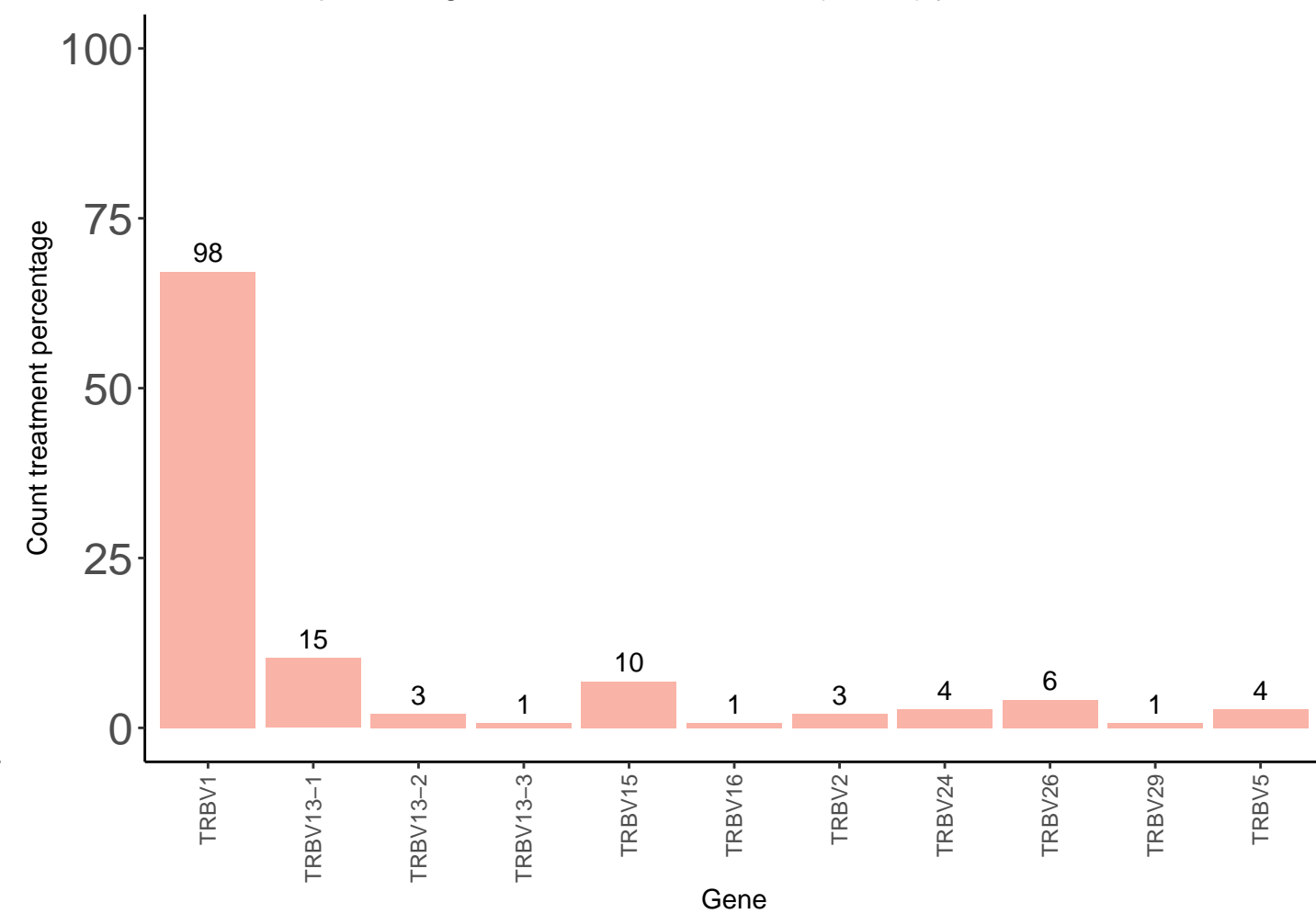
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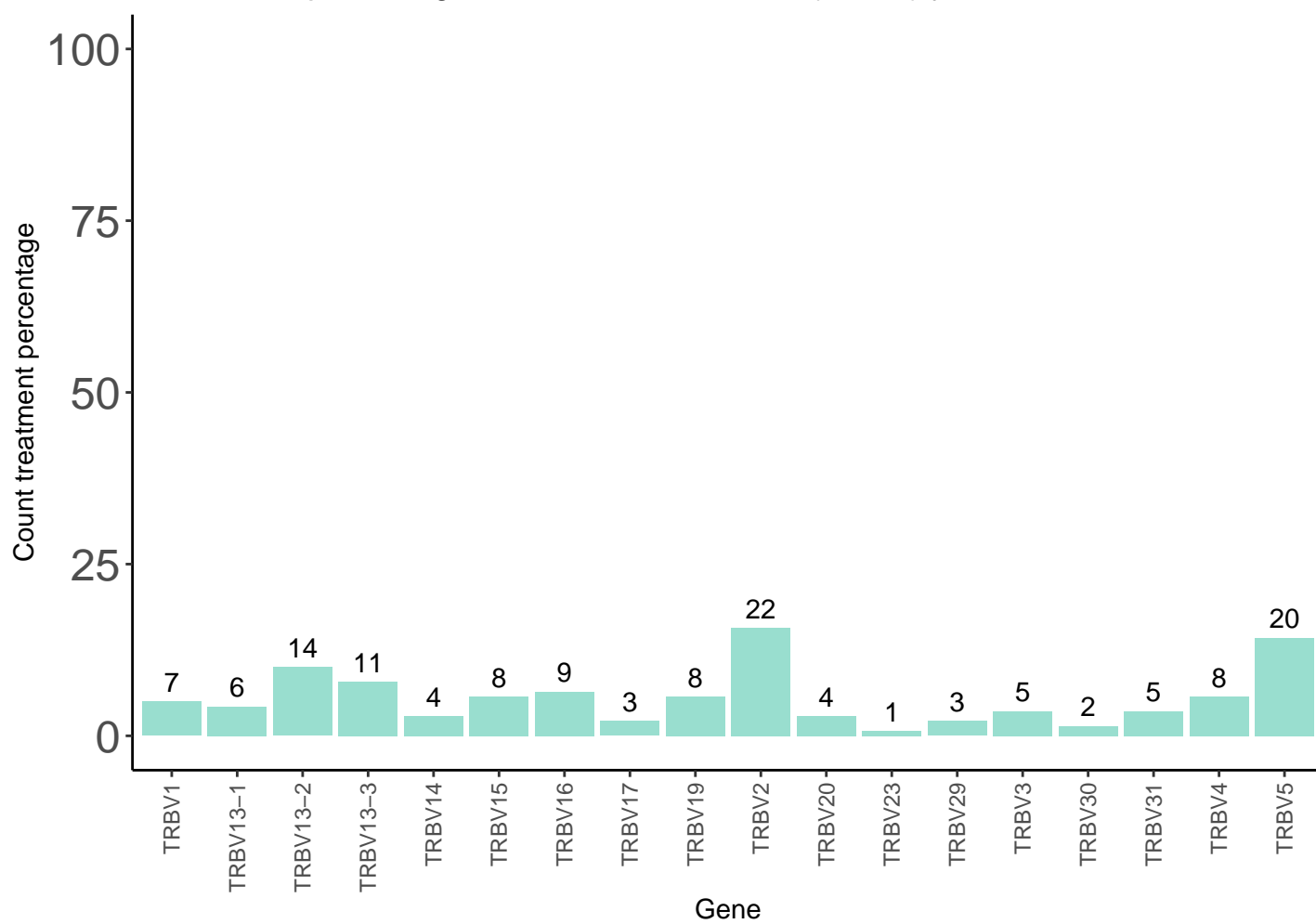
Gene count percentage Beta Genes: Control\_Tet- | Total: 117



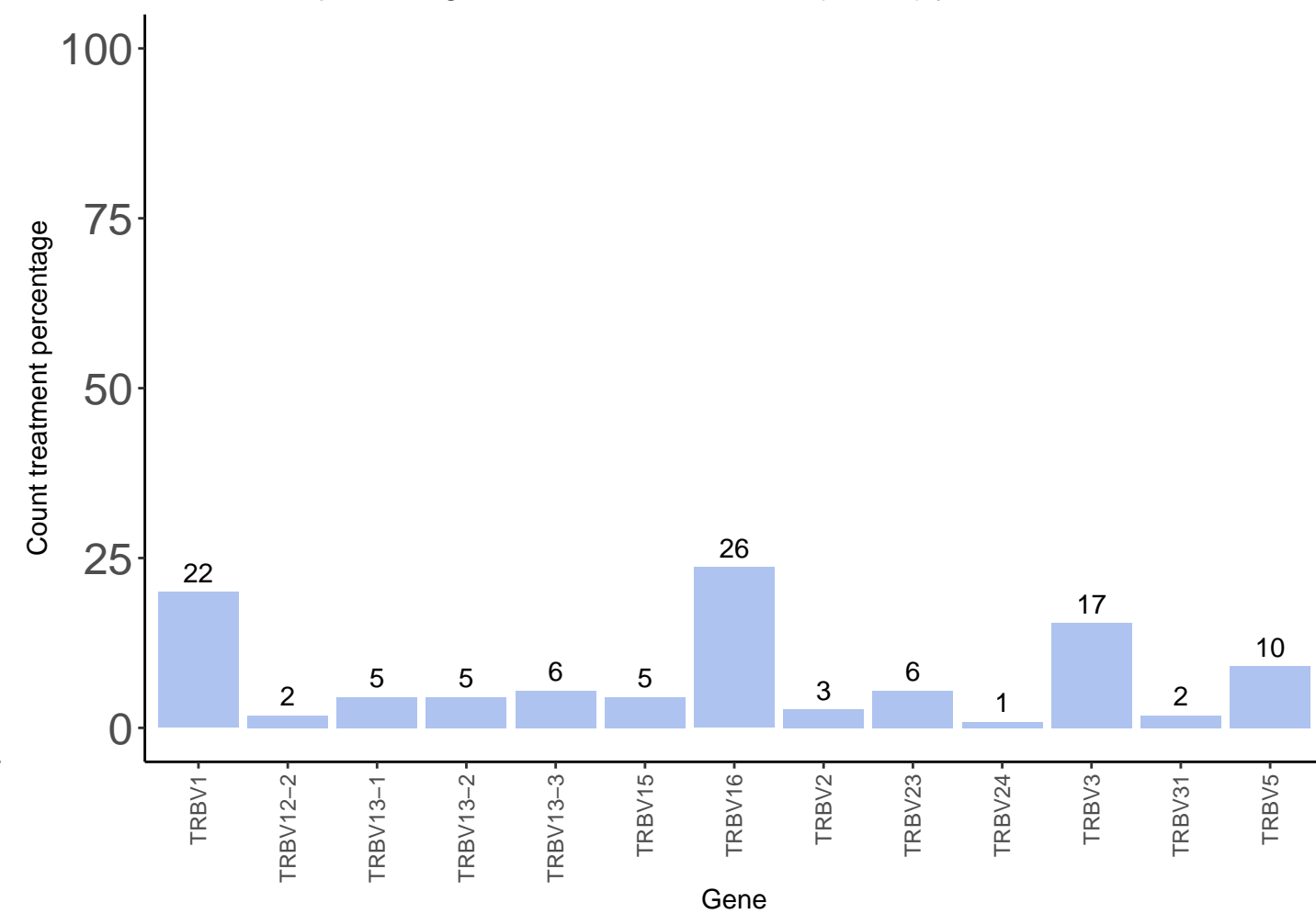
Gene count percentage Beta Genes: Tet+\_InsB(10-23) | Total: 146



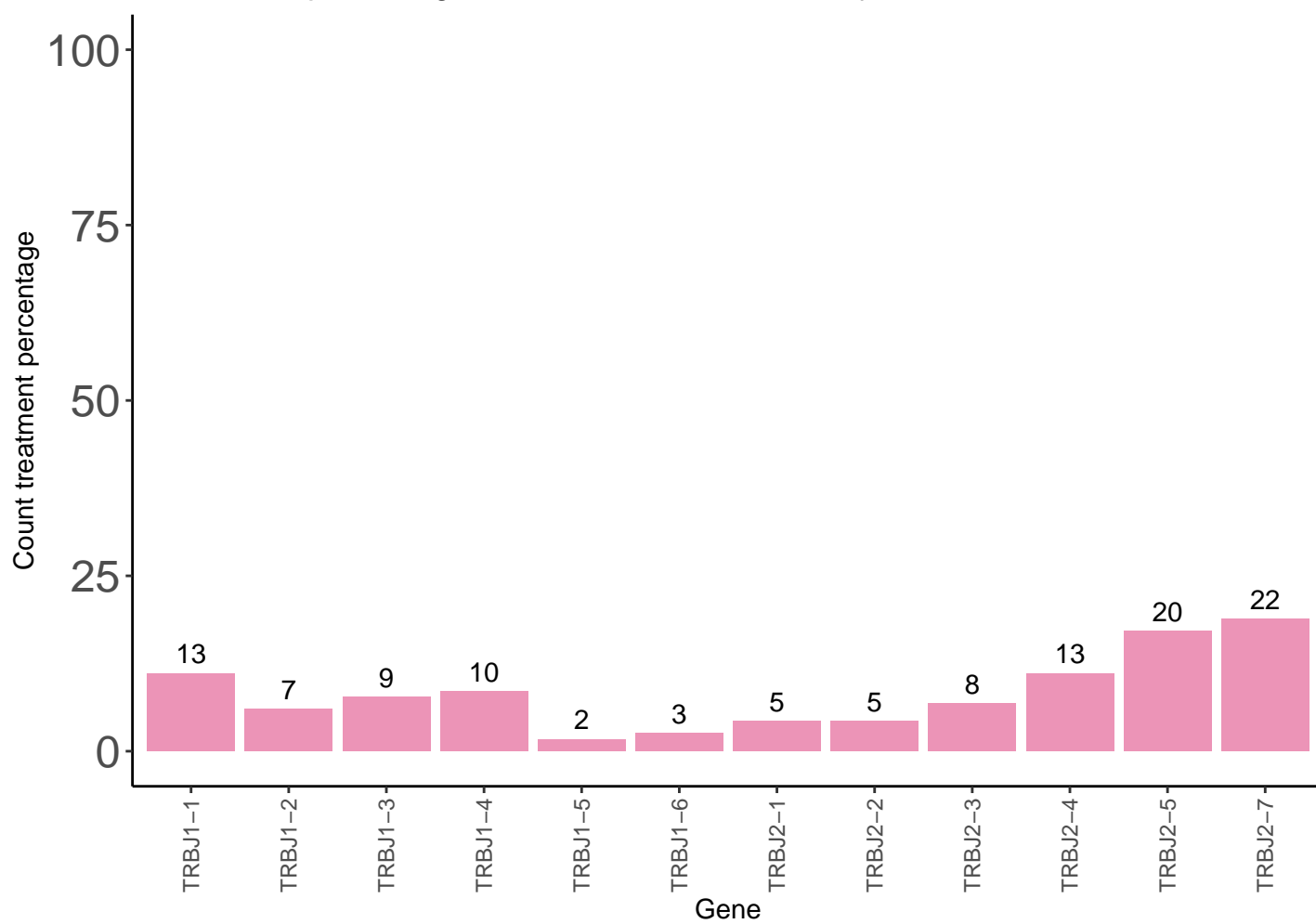
Gene count percentage Beta Genes: Tet+\_InsB(12-20) | Total: 140



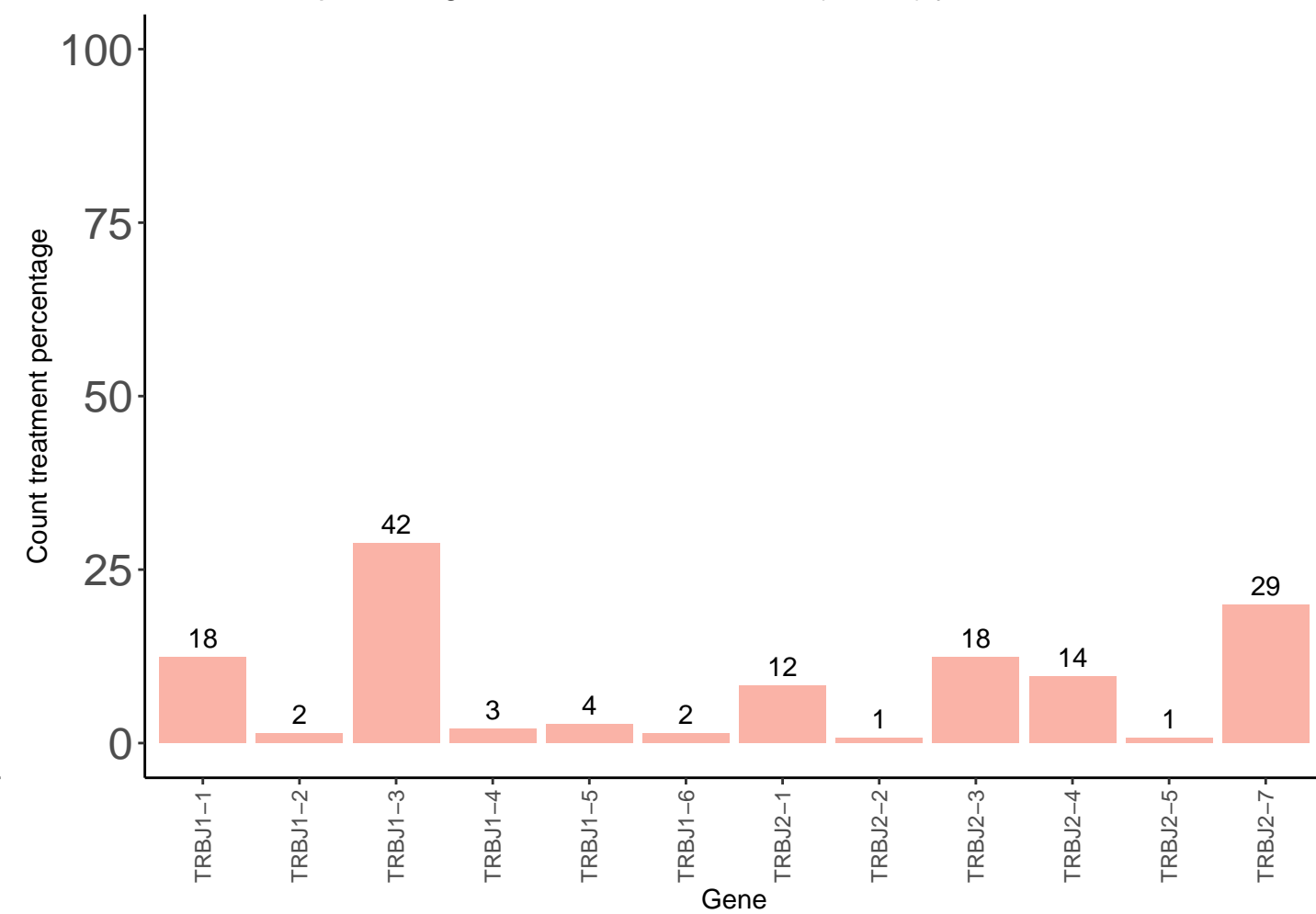
Gene count percentage Beta Genes: Tet+\_InsB(13-21) | Total: 110



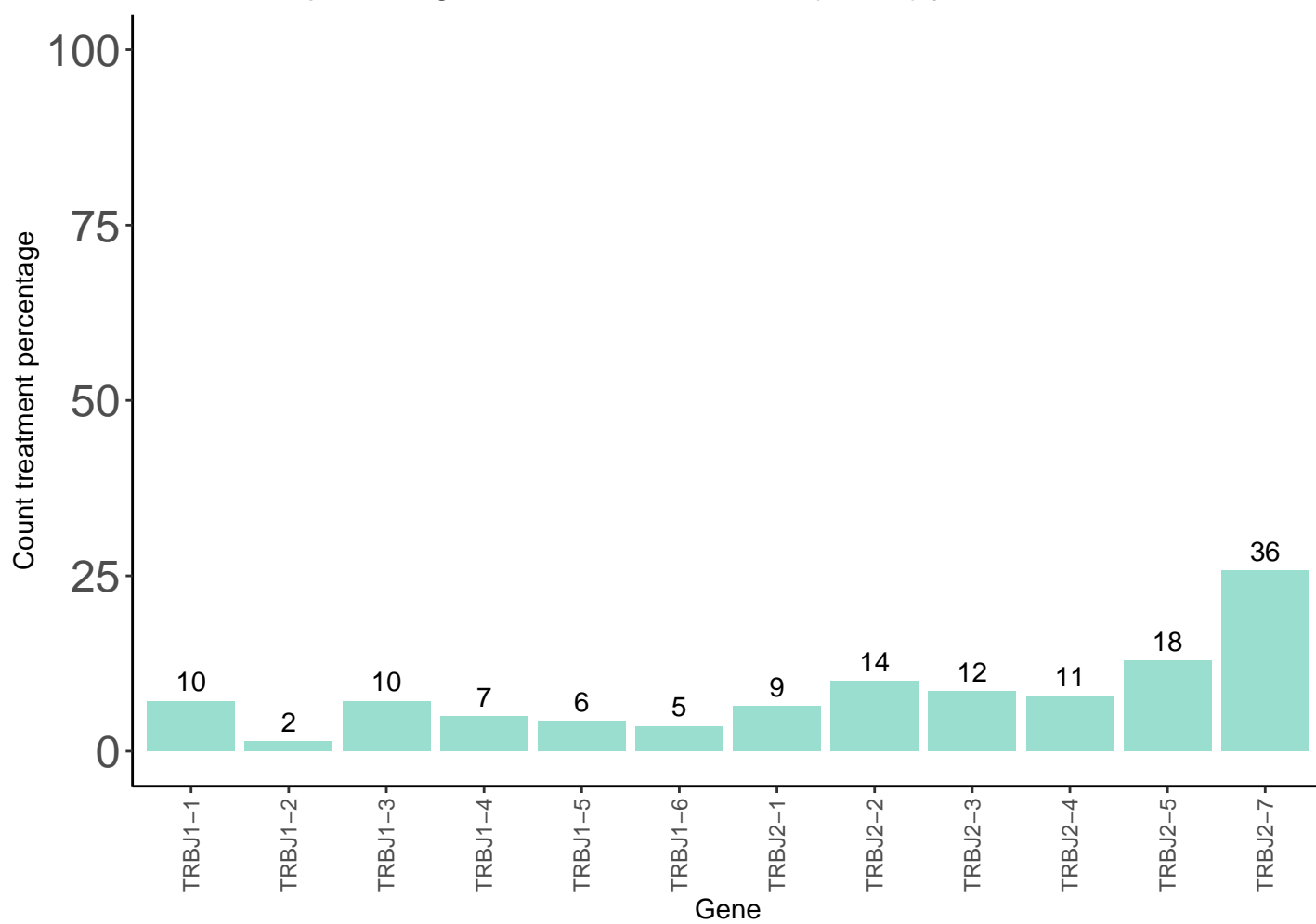
Gene count percentage Beta Genes: Control\_Tet- | Total: 117



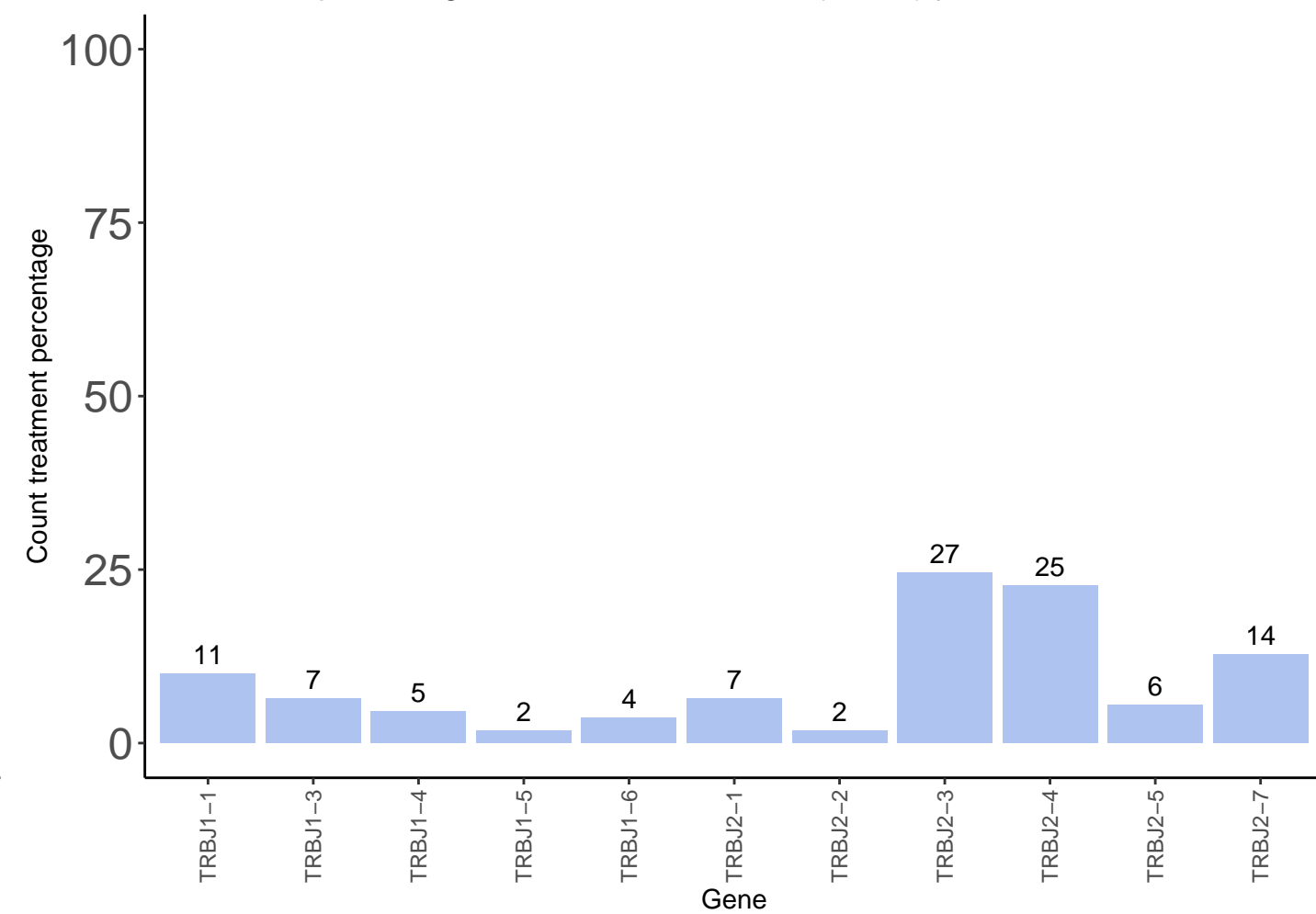
Gene count percentage Beta Genes: Tet+\_InsB(10-23) | Total: 146



Gene count percentage Beta Genes: Tet+\_InsB(12-20) | Total: 140

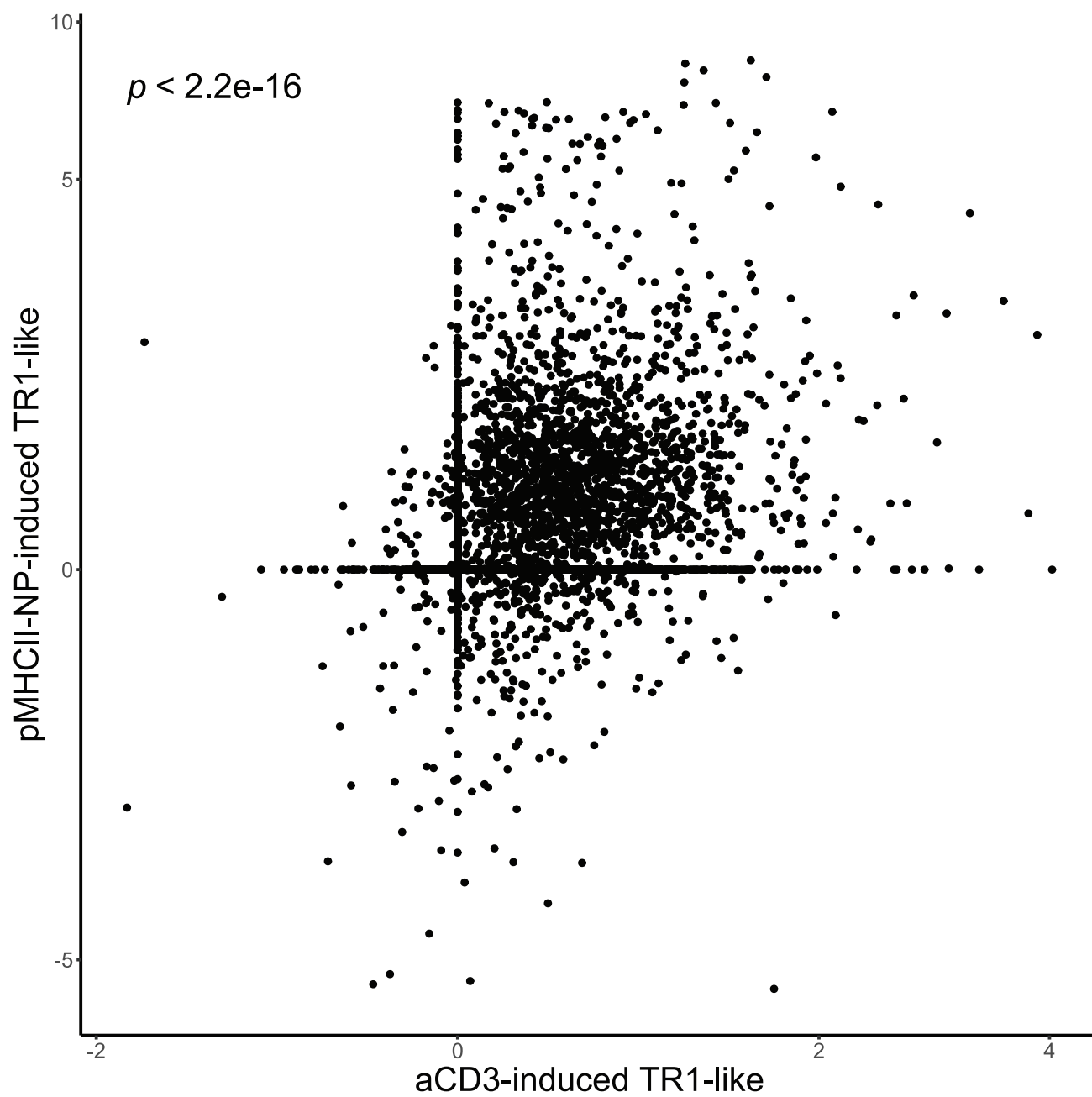


Gene count percentage Beta Genes: Tet+\_InsB(13-21) | Total: 110



**Supplementary Figure 2. TRAV, TRAJ, TRBV and TRBJ usage.** Histogram plots comparing the number of TCR $\alpha$  and TCR $\beta$  sequences carrying different V $\alpha$ , J $\alpha$ , V $\beta$  and J $\beta$ -coding elements.

Suppl. Fig. 3





**Supplementary Figure 3. pMHCII-NP-induced TR1-like cells are transcriptionally similar to anti-CD3 mAb-induced TR1-like cells.** Correlation between the levels of gene expression between TR1-like (cluster #2) cells from mice treated with InsB<sub>12-20</sub>-CT-R1/IA<sup>g7</sup>-NP, InsB<sub>13-21</sub>-R2/IA<sup>g7</sup>-NP, InsB<sub>10-23</sub>-CT-R3/IA<sup>g7</sup>-NP and BDC2.5mi/IA<sup>g7</sup>-NP (cluster #2) and the TR1-like cells induced by anti-CD3 mAb (cluster #2 in ref. 5) (relative to Tconv cells). The P value refers to the Pearson correlation coefficient.