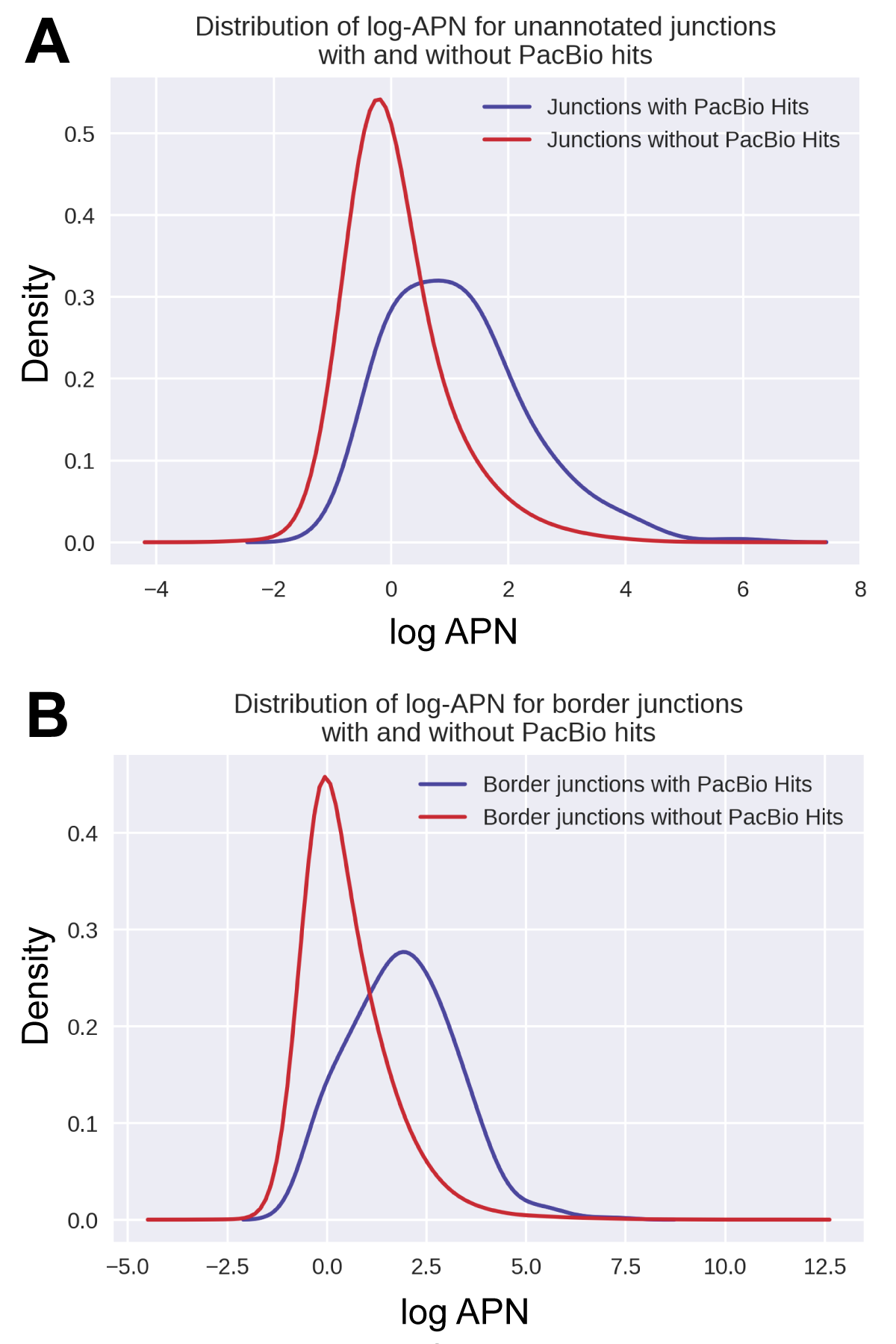
**Supplementary Table 1. All other possible, logical splice junctions derived from the gene model in Figure 1 example**

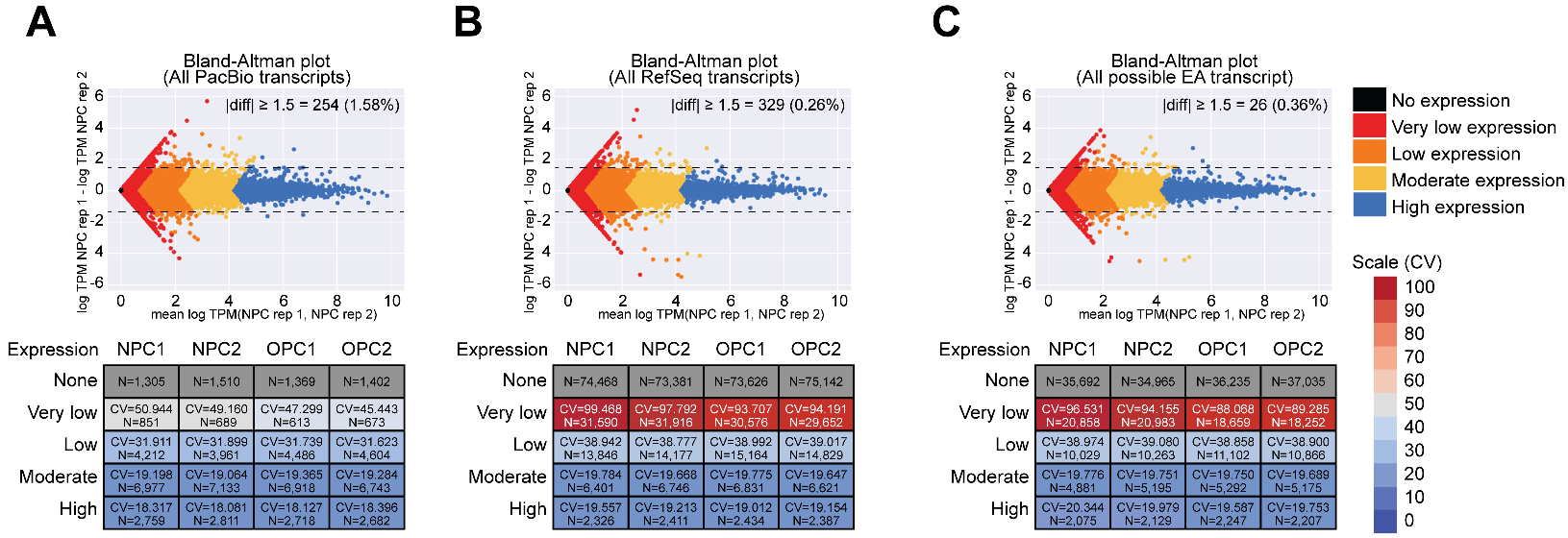
|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Splice junction a** | **Isoform** | **Annotated? (Y/N)** | **Annotated frequency (unique, common, constitutive)** | **Exon-skipping? (Y/N)** | **Alternative donor? (Y/N)** | **Alternative acceptor? (Y/N)** | **Exon-intron border? (Y/N)** |
| Exon A:Exon D | Isoform 1 | Y | Unique | N | Y | N | N |
| Exon B:Exon D | Isoform 2 | Y | Unique | N | Y | N | N |
| Exon C:Exon D | Isoform 3 | Y | Unique | N | Y | N | N |
| Exon D:Exon E | Isoforms 1, 2 and 3 | Y | Constitutive | N | N | N | N |
| Exon E:Exon F|Exon E:Exon G\* | Isoform 1 (E:G), Isoform 2 (E:F) | Y | Common | N | N | N | N |
| Exon E:Exon I | Isoform 3 | Y | Unique | Y | N | N | N |
| Exon F:Exon I | Isoform 2 | Y | Unique | Y | Y | N | N |
| Exon G:Exon H | Isoform 1 | Y | Unique | N | Y | N | N |
| Exon H:Exon J | Isoform 1 | Y | Unique | Y | N | Y | N |
| Exon I:Exon K | Isoform 3 | Y | Unique | N | N | Y | N |
| Exon I:Exon L | Isoform 2 | Y | Unique | N | N | Y | N |
| Exon A:Exon E |  | N | n/a | Y | Y | N | N |
| Exon B:Exon E |  | N | n/a | Y | Y | N | N |
| Exon C:Exon E |  | N | n/a | Y | Y | N | N |
| Exon A:Exon F|Exon A:Exon G\* |  | N | n/a | Y | Y | N | N |
| Exon B:Exon F|Exon B:Exon G\* |  | N | n/a | Y | Y | N | N |
| Exon C:Exon F|Exon C:Exon G\* |  | N | n/a | Y | Y | N | N |
| Exon A:Exon H |  | N | n/a | Y | Y | N | N |
| Exon B:Exon H |  | N | n/a | Y | Y | N | N |
| Exon C:Exon H |  | N | n/a | Y | Y | N | N |
| Exon A:Exon I |  | N | n/a | Y | Y | N | N |
| Exon B:Exon I |  | N | n/a | Y | Y | N | N |
| Exon C:Exon I |  | N | n/a | Y | Y | N | N |
| Exon A:Exon J |  | N | n/a | Y | Y | Y | N |
| Exon A:Exon K |  | N | n/a | Y | Y | Y | N |
| Exon A:Exon L |  | N | n/a | Y | Y | Y | N |
| Exon B:Exon J |  | N | n/a | Y | Y | Y | N |
| Exon B:Exon K |  | N | n/a | Y | Y | Y | N |
| Exon B:Exon L |  | N | n/a | Y | Y | Y | N |
| Exon C:Exon J |  | N | n/a | Y | Y | Y | N |
| Exon C:Exon K |  | N | n/a | Y | Y | Y | N |
| Exon C:Exon L |  | N | n/a | Y | Y | Y | N |
| Exon D:Exon F|Exon D:Exon G\* |  | N | n/a | Y | N | N | N |
| Exon D:Exon H |  | N | n/a | Y | N | N | N |
| Exon D:Exon I |  | N | n/a | Y | N | N | N |
| Exon D:Exon J |  | N | n/a | Y | N | Y | N |
| Exon D:Exon K |  | N | n/a | Y | N | Y | N |
| Exon D:Exon L |  | N | n/a | Y | N | Y | N |
| Exon E:Exon H |  | N | n/a | Y | N | N | N |
| Exon E:Exon I |  | N | n/a | Y | N | N | N |
| Exon E:Exon J |  | N | n/a | Y | N | Y | N |
| Exon E:Exon K |  | N | n/a | Y | N | Y | N |
| Exon E:Exon L |  | N | n/a | Y | N | Y | N |
| Exon F:Exon H |  | N | n/a | Y | Y | N | N |
| Exon G:Exon H |  | N | n/a | Y | Y | N | N |
| Exon F:Exon I |  | N | n/a | Y | Y | N | N |
| Exon G:Exon I |  | N | n/a | Y | Y | N | N |
| Exon F:Exon J |  | N | n/a | Y | Y | Y | N |
| Exon F:Exon K |  | N | n/a | Y | Y | Y | N |
| Exon F:Exon L |  | N | n/a | Y | Y | Y | N |
| Exon G:Exon J |  | N | n/a | Y | Y | Y | N |
| Exon G:Exon K |  | N | n/a | Y | Y | Y | N |
| Exon G:Exon L |  | N | n/a | Y | Y | Y | N |
| Exon H:Exon I |  | N | n/a | N | N | N | N |
| Exon H:Exon K |  | N | n/a | Y | N | Y | N |
| Exon H:Exon L |  | N | n/a | Y | N | Y | N |
| Exon I:Exon J |  | N | n/a | N | N | Y | N |
| Exon C donor:intron |  | N | n/a | N | Y | N | Y |
| Intron:Exon D acceptor |  | N | n/a | N | N | N | Y |
| Exon D donor:intron |  | N | n/a | N | N | N | Y |
| Intron:Exon E acceptor |  | N | n/a | N | N | N | Y |
| Exon E donor:intron |  | N | n/a | N | N | N | Y |
| Intron:Exon F acceptor|Intron:Exon G acceptor \* |  | N | n/a | N | N | N | Y |
| Exon G donor:intron |  | N | n/a | N | Y | N | Y |
| Exon H acceptor:intron |  | N | n/a | N | N | N | Y |
| Exon H donor:intron |  | N | n/a | N | N | N | Y |
| Exon I acceptor:intron |  | N | n/a | N | N | N | Y |
| Exon I donor:intron |  | N | n/a | N | N | N | Y |
| Exon J acceptor:intron |  | N | n/a | N | N | Y | Y |

a Event ID is denoted with the 5’most exon/intron first. The second exon/intron is separated from the first using a colon. Events with identical donors and acceptors are separated by a “|”

\* Junction is not unique as exons F and G share the same acceptor site

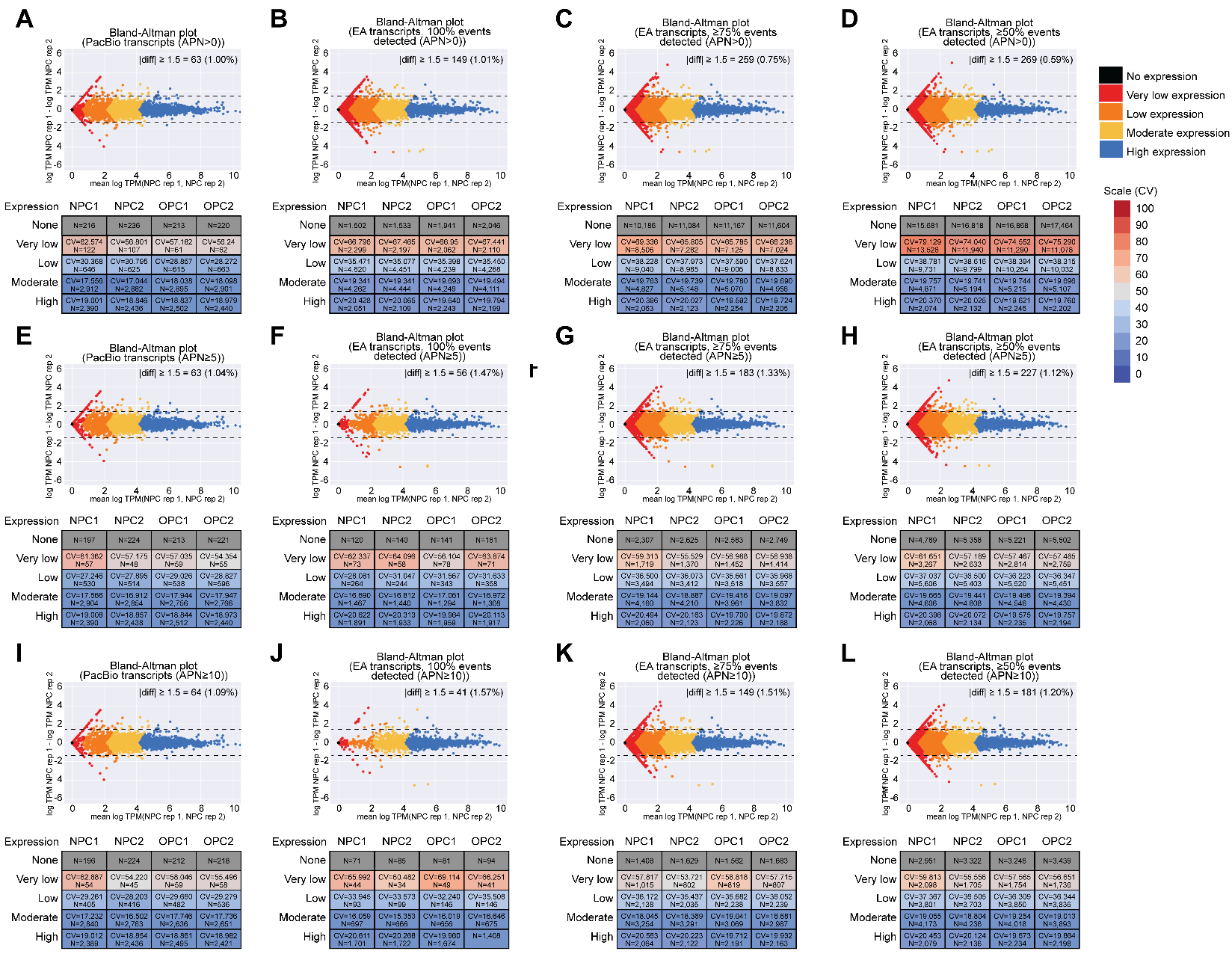


**Supplementary Figure 1. Distribution of coverage of unannotated splicing events (APN>0).** Density plot of the log-APN distribution between detected unannotated junctions (A) and border junctions (D), with and without BLAST hits to the PacBio transcriptome: 204 unannotated junctions with BLAST hits, 8,208 unannotated junctions without BLAST hits, 804 border junctions with BLAST hits, and 26,688 border junctions without BLAST hits.

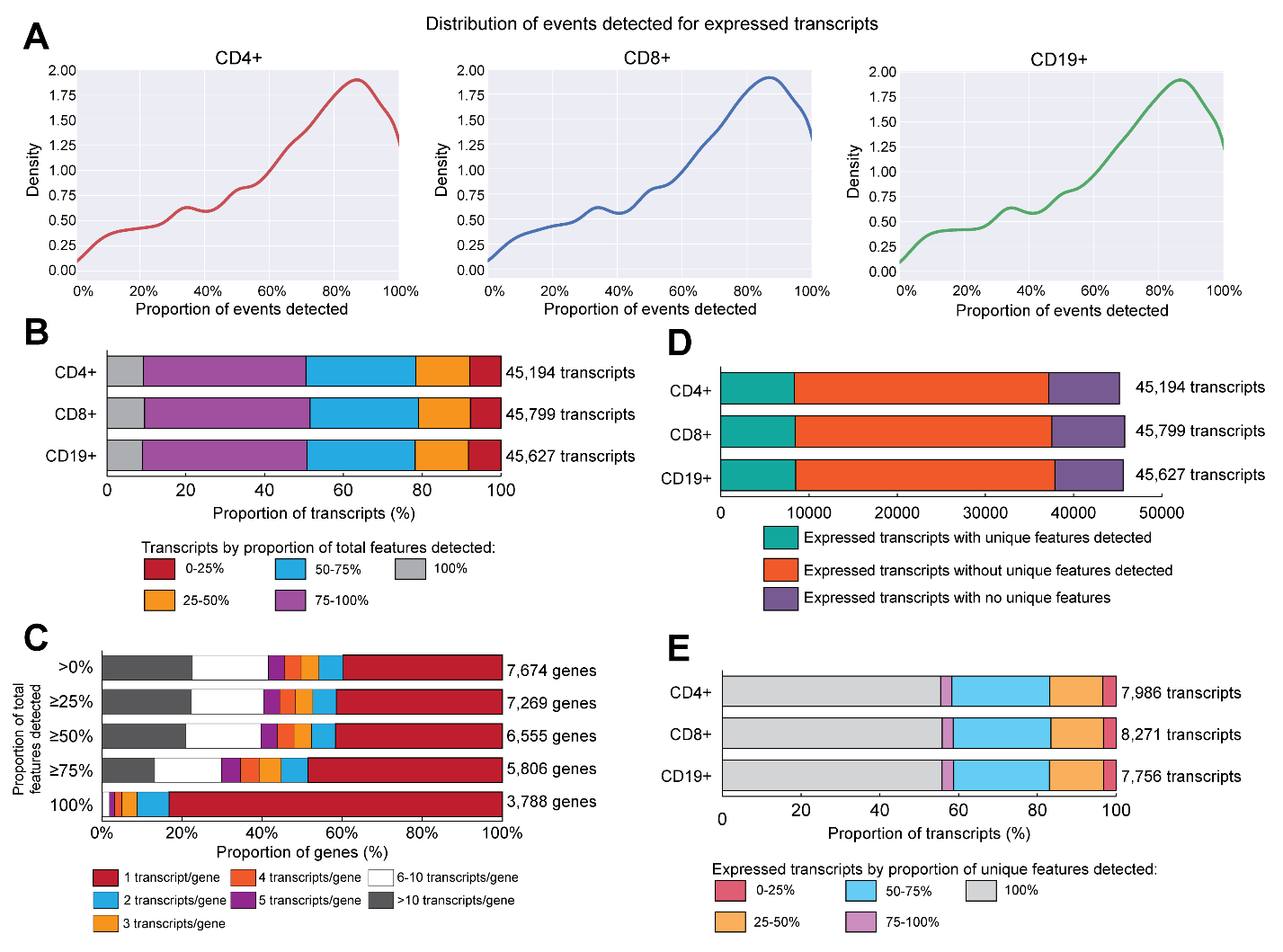
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**Supplementary Figure 2.** Replicate-to-replicate concordance of RSEM transcript estimates between PacBio, RefSeq and Event Analysis transcripts. Bland-Altman plots and coefficients of variance (CVs) for (A) all PacBio transcripts (16,104 transcripts) (B) all RefSeq transcripts (128,631 transcripts) (C) all possible Event Analysis transcripts (73,437 transcripts). Transcripts are binned into no expression (log-TPM = 0; black), very low expression (0 < log-TPM < 0.5; red), low expression (0.5 ≤ log-TPM < 2; orange), moderate expression (2 ≤ log-TPM < 4; yellow), and high expression (log-TPM ≥ 4; blue) and the CVs for each bin and for each sample (NPC rep 1, NPC rep 2, OPC rep 1, OPC rep 2) are indicated. For Bland-Altman plots, transcripts are binned based on the lowest expression of either NPC replicate.

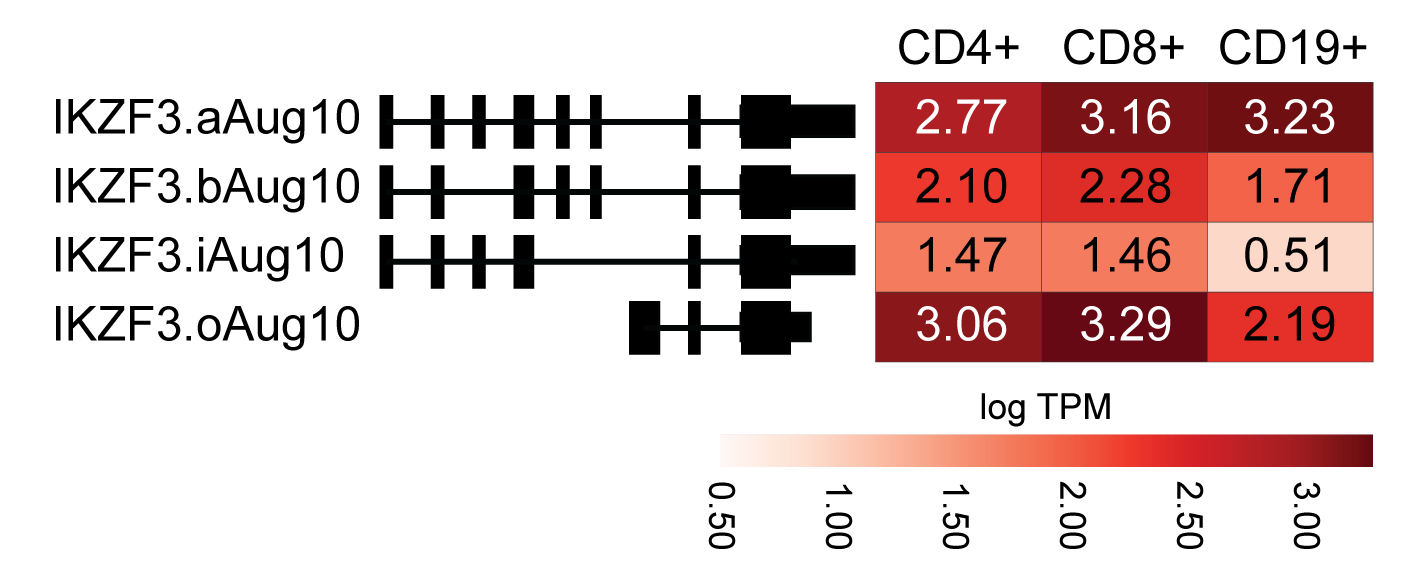
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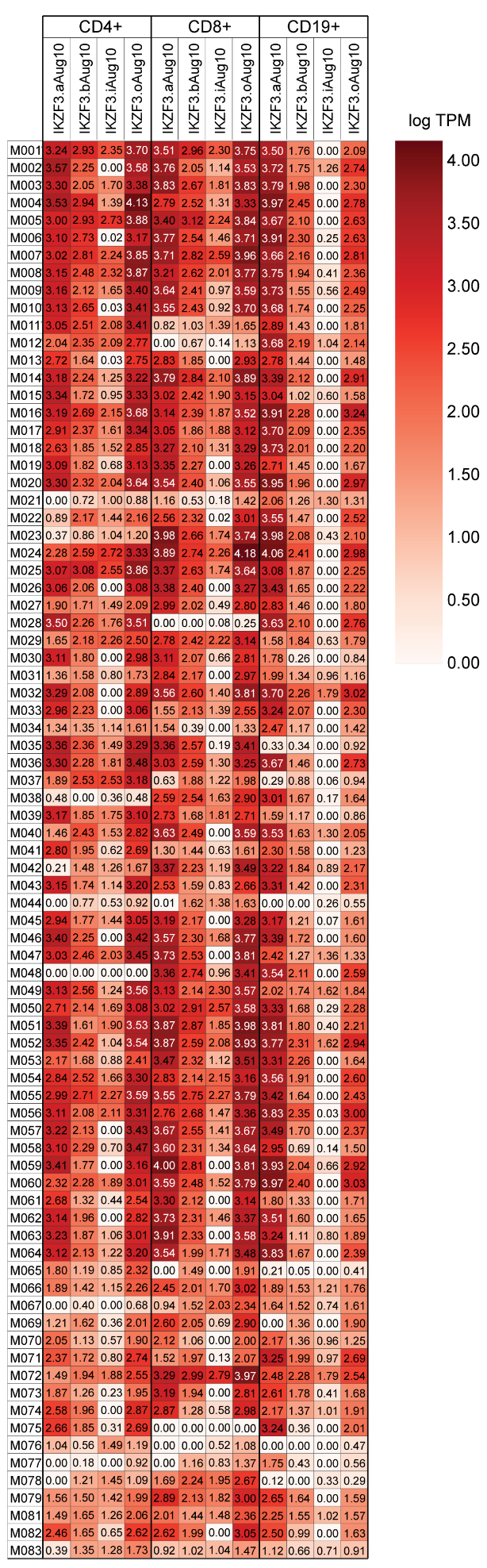
**Supplementary Figure 3.** Replicate-to-replicate concordance of RSEM transcript estimates by event detection threshold (APN>0, ≥5, ≥10) and proportion of events detected. Bland-Altman plots and coefficients of variance (CVs) for (A) PacBio transcripts (APN>0; N=6,286); (B) Event Analysis (EA) transcripts with 100% of events detected (APN>0; N=14,734); (C) EA transcripts with at least 75% of events detected (APN>0; N=34,622); (D) EA transcripts with at least 50% of events detected (APN>0; N=45,883); (E) PacBio transcripts (APN≥5; N=6,078); (F) EA transcripts with 100% of events detected (APN≥5; N=3,815); (G) EA transcripts with at least 75% of events detected (APN≥5; N=13,740); (H) EA transcripts with at least 50% of events detected (APN≥5; N=20,336); (I) PacBio transcripts (APN≥10; N=5,884), (J) EA transcripts with 100% of events detected (APN≥10; N=2,606); (K) EA transcripts with at least 75% of events detected (APN≥10; N=9,879); (L) EA transcripts with at least 50% of events detected (APN≥10; N=15,102). Transcripts are binned into no expression (log-TPM = 0; black), very low expression (0 < log-TPM < 0.5; red), low expression (0.5 ≤ log-TPM < 2; orange), moderate expression (2 ≤ log-TPM < 4; yellow), and high expression (log-TPM ≥ 4; blue) and the CVs for each bin and for each sample (NPC rep 1, NPC rep 2, OPC rep 1, OPC rep 2) are indicated. For Bland-Altman plots, transcripts are binned based on the lowest expression of either NPC replicate.

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**Supplementary Figure 4. Distribution of the total events detected per transcript in the T1D case-only data.** (A) Density plot of the distribution of proportion of total events detected for CD4+, CD8+ and CD19+ lymphocytes. (B) Proportion of transcripts by the proportion of total events detected. (C) Distribution of number of transcripts detected per gene. (D) The proportions of transcripts with at least one unique event detected, transcripts with unique events but none detected, and transcripts with no assigned unique events. (E) Distribution of the expressed transcripts with at least one unique event detected by the proportion of unique events detected.

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**Supplementary Figure 5.** Log mean TPM of four *IKZF3* AceView transcripts from the reduced transcriptome for each cell type (CD4+, CD18+ and CD19+ lymphocytes) from the T1D case-only data. The most expressed *IKZF3* transcript is different between T cells (IKZF3.oAug10) and B cells (IKZF3.aAug10). Introns in transcript models are not drawn to scale.

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**Supplementary Figure 6.** Log TPM of four *IKZF3* AceView transcripts from the reduced transcriptome for each cell type (CD4+, CD8+, and CD19+ lymphocytes) for each subject from the T1D case-only data. While there is variability between subjects for the estimates of each transcript, the transcript IKZF3.iAug10 is almost completely absent in CD19+ lymphocytes.