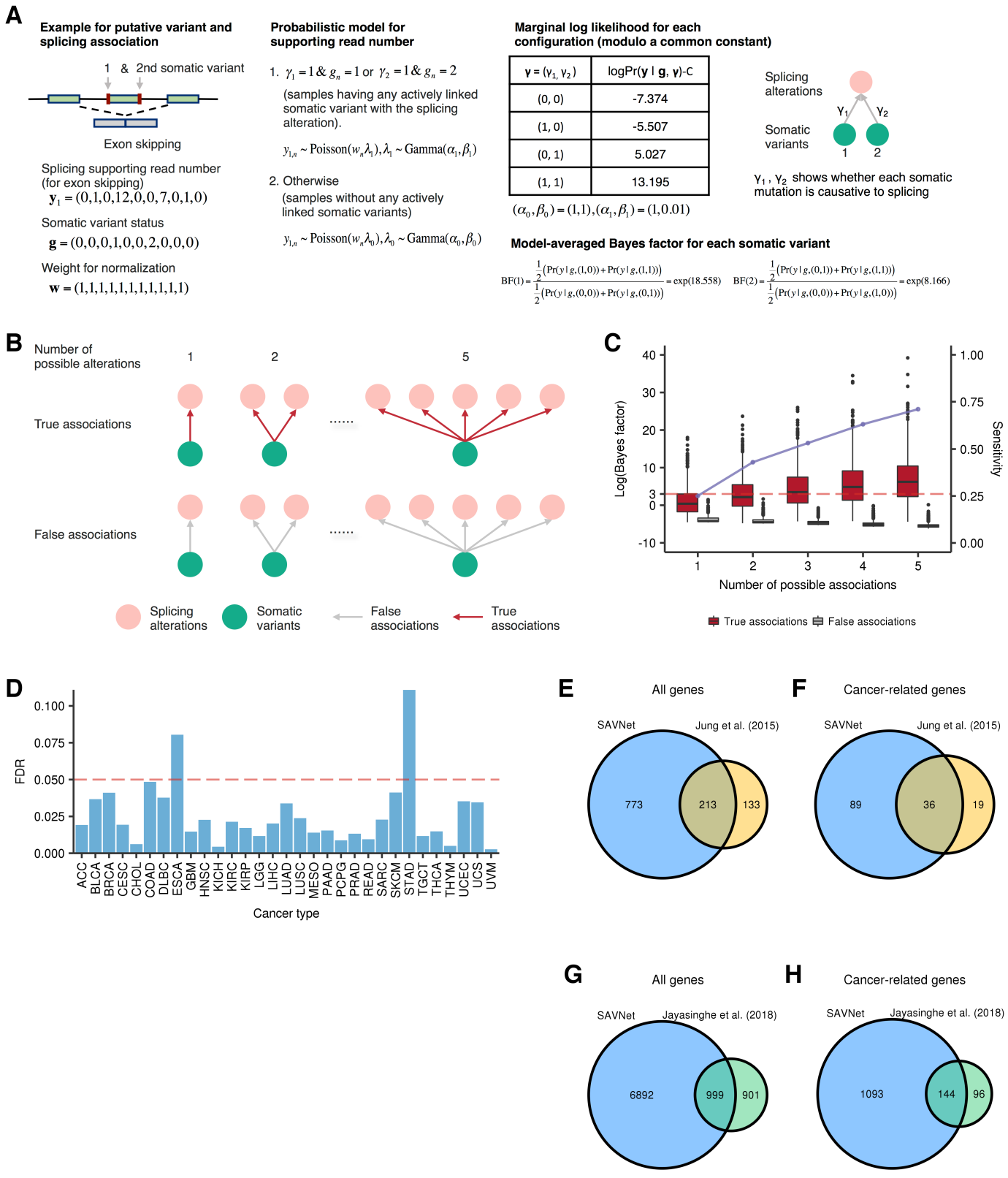

Supplementary Figure 1: Evaluation of SAVNet performance.

(A) An example of calculating the Bayes factor for the association between somatic variants and a splicing alteration using SAVNet. **(B)** An illustration of a simulation study on the effect of the number of potentially associated splicing alterations on the performance of SAV detection. The numbers of splicing-supporting reads are generated by Poisson distribution with parameters of 3 or 0.3 when splicing alterations are actually associated (true) or not associated (false) with a somatic variant, respectively. Here, we assume an

all-or-nothing situation: either all possible splicing alterations or none are associated with a somatic variant. For each group, 100 trials with 20 samples were performed. **(C)** Box plots showing the logarithm of the Bayes factor for each number of true (red) and false (gray) variant-splicing associations. Also, the sensitivity (the fraction of trials where the logarithm of the Bayes factor was greater than 3.0 and the default threshold used in this study) is shown in purple points with lines for the true association group. As the number of associated splicing alterations increases, the sensitivity improves dramatically. On the other hand, the logarithm of the Bayes factor for the false association group does not reach the threshold irrespective of the number of associated splicing alterations, indicating the high specificity of SAVNet. **(D)** FDR for each cancer type estimated by permutation of combinations of WES and RNA-seq data when the threshold of the logarithm of the Bayes factor was set to 3.0. For ESCA and STAD, the thresholds were adjusted so that their FDRs were maintained below 0.05. **(E, F)** Venn diagrams showing the overlap of SAVs detected by the current (SAVNet) and previous (ratio-based splicing analysis) studies (Jung et al. 2015). SAVs at positions analyzed by both studies (−1, +1, and +2 of donor and acceptor sites) were evaluated for all genes **(E)** and candidate cancer-related genes (Ye et al. 2016) **(F)**. **(G, H)** Venn diagrams showing the overlap of SAVs detected by the current (SAVNet) and previous (MiSplice) studies (Jayasinghe et al. 2018). SAVs were evaluated for all genes **(G)** and candidate cancer-related genes (Ye et al. 2016) **(H)**.