

Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: **FLAIR transcript models derived from nanopore sequencing data.** GTF file containing isoforms assembled from the FLAIR pipeline using all nanopore data generated from this study with a supporting read threshold of 3.

File Name: Supplementary Data 2

Description: **Isoform annotations in an extended PSL format for isoforms assembled from the FLAIR pipeline.** Each row is a FLAIR isoform. The first 21 columns follow PSL format, and columns after 21 contain additional information for each isoform. Spliced or intron retaining-isoforms are indicated with a 0 or 1 in column 22; productivity using the first start codon available in column 23; productivity using the longest ORF in column 24; the CLL SF3B1WT 1-3, CLL SF3B1K700E 1-3, and B cell samples 1-3 normalized isoform expression levels are in columns 25-33. The productivity categories productive, unproductive, no start codon, and no stop codon are indicated with PRO, PTC, NGO, and NST respectively.

File Name: Supplementary Data 3

Description: **Alternative splicing events identified using nanopore sequencing data.** The alternative splicing events identified by FLAIR diffSplice and DRIMSeq that had p-values < 0.1 and abs(dPSI) > 10.

File Name: Supplementary Data 4

Description: Differentially used isoforms identified using nanopore sequencing data. Differentially used isoforms as identified using FLAIR diffExp with p-value < 0.1 and abs(dPSI) > 10, correcting for batches as specified in Supplementary Table 2.

File Name: Supplementary Data 5

Description: **GO enrichment of genes with intron retention downregulated in SF3B1K700E relative to SF3B1WT determined by nanopore sequencing data.** GOseq results, with only GO terms with overrepresented p-values < 0.05 included.