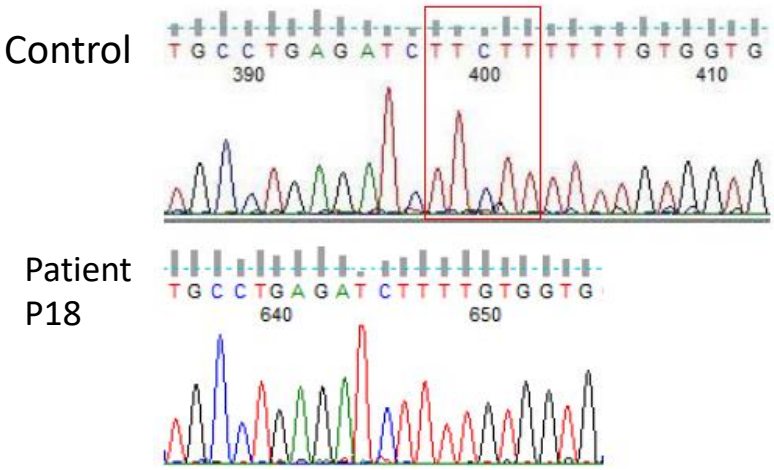


Fig. S1. 5 bp deletion confirmed by Sanger Sequencing in patient P18.

Sanger Sequencing of *CLCNKB* exon 9 in P18 (lower panel) and a control (upper panel). The 5 bp deletion appears homozygous because of the *CLCNKB* deletion allele F *in trans*.

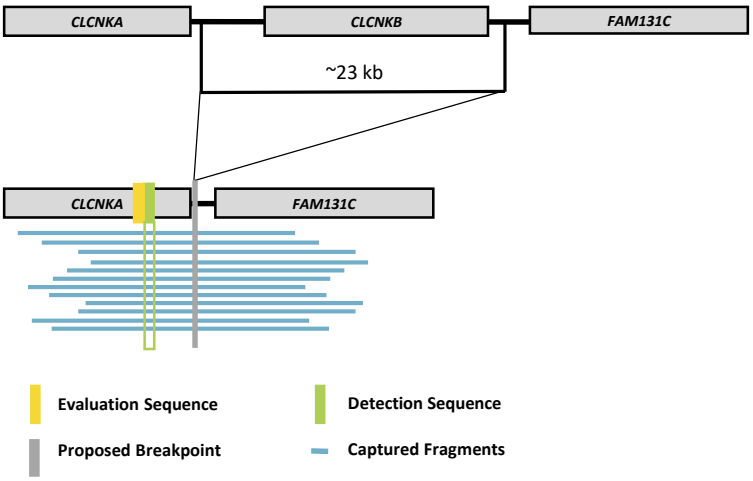


Fig. S2. Schematic view of the Samplix Xdrop custom sequence capture design.

Detection and evaluation sequence designed in *CLCNKA* to capture up to 50 kb of HMW genomic DNA fragments covering *CLCNKA* and *CLCNKB*. Proposed breakpoints in the region between *CLCNKA* and *CLCNKB*.

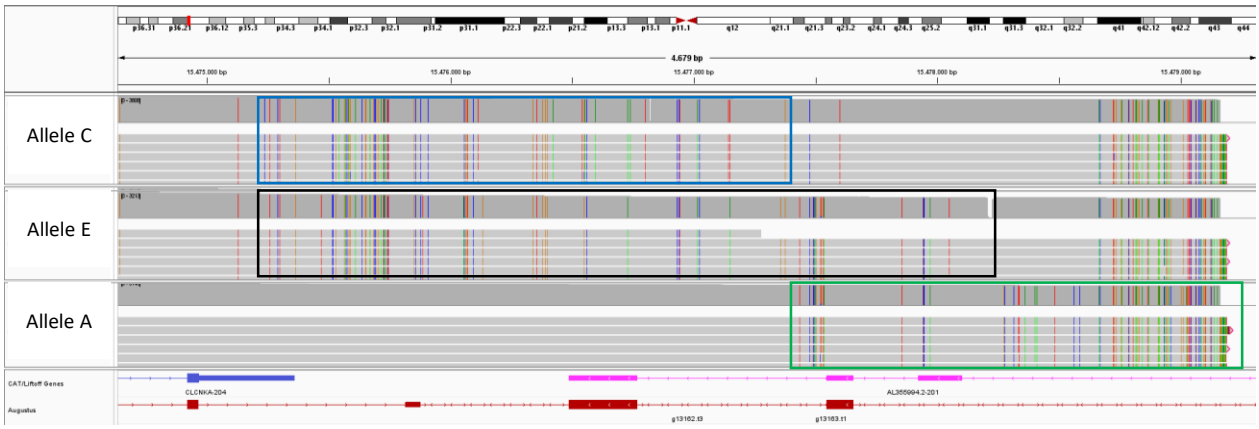
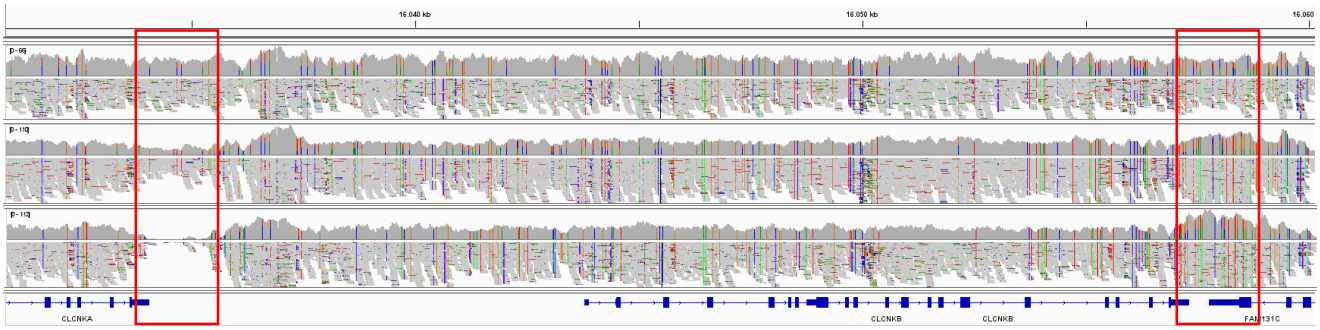


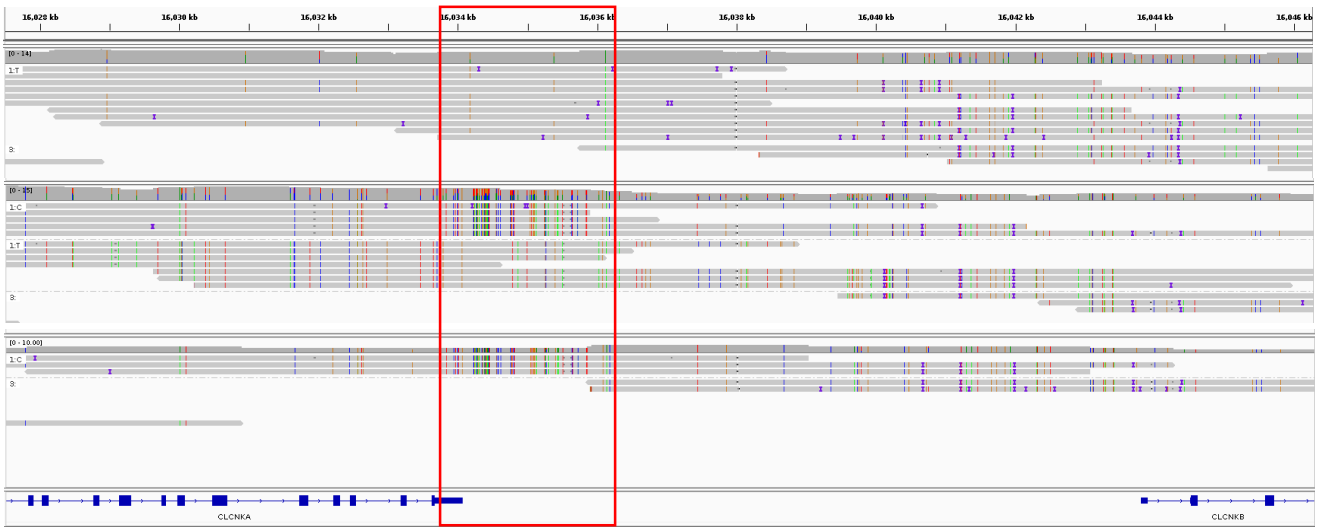
Fig. S3. T2T CHM13-v.2.0 alignment

Sequence alignment data of the *CLCNKA* 3‘UTR from three patients, aligned to the T2T CHM13-v2.0 reference genome, illustrating the transposition haplotype structure. The smaller ~2.2 kb sequence transposition haplotype is indicated by the blue box. The larger ~3 kb sequence transposition is indicated by the black box. The *CLCNKB* sequence after the single breakpoint region in allele A (allele without transposition haplotype) is indicated by the green box.

A


i
ii
iii
CLCNKA
CLCNKB
CLCNKB
FAM131C

B


i
ii
iii
CLCNKA
CLCNKB

C

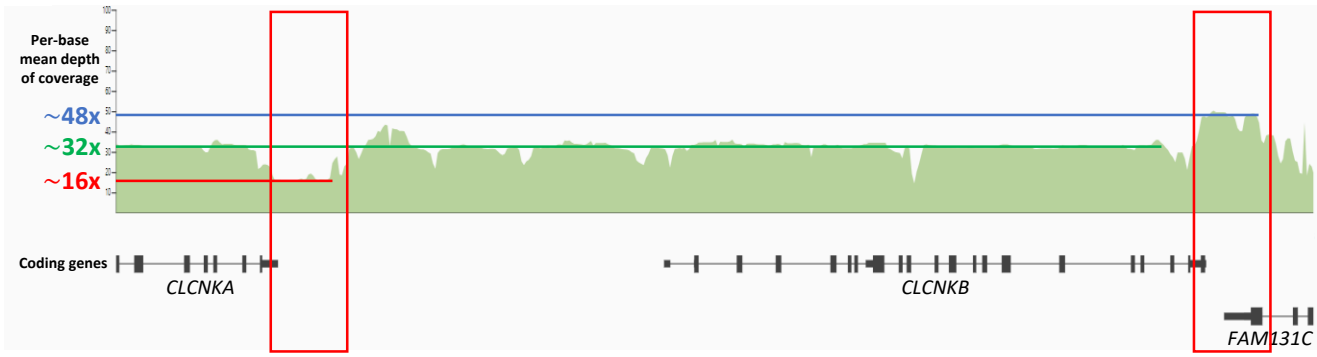

Per-base mean depth of coverage
~48x
~32x
~16x
Coding genes
CLCNKA
CLCNKB
FAM131C

Fig. S4. Workup of the *CLCNKA* 3’ UTR sequence transposition haplotype found in this study.

CLCNKA 3’ UTR sequence transposition haplotype in short- and long-read whole genome in-house *CLCNKB* deletion control datasets. Whole genome data of the reference (i) and the heterozygous (ii) and homozygous (iii) variant haplotype, respectively. Sequences are visualized in IGV. Genes are indicated in blue; Exons are indicated as vertical bars; Gene orientation is indicated by arrows. Genomic coordinates refer to the hg38 human reference. **A** In the short-read alignment, the duplicated 2.2-3 kb 3’ UTR of *CLCNKB* are aligned in the *CLCNKB* 3’ UTR (right red square), leading to a coverage gain in the variant haplotype carriers. The loss of the 3’ UTR of *CLCNKA* is indicated by the reduced coverage (left red square). **B** In the long-read alignment, the inserted *CLCNKB* 3’ UTR fragment (red square) is indicated by the differentiating nucleotides that distinguish the *CLCNKA* 3’ UTR and the *CLCNKB* 3’ UTR. **C** Coverage plot of the *CLCNKA*/*CLCNKB* gene locus adapted from gnomAD (3.1.2). Reduced coverage depth in the *CLCNKA* 3’ UTR (left red square) and elevated coverage in the *CLCNKB* 3’ UTR (right red square) are visible in the normal population data. This data indicates a 2.2-3 kb loss of *CLCNKA* 3’ UTR sequence and a duplication of the *CLCNKB* 3’ UTR sequence in approximately 50 % of control alleles, corresponding to the expected representation of the transposition haplotype in short-read NGS data.

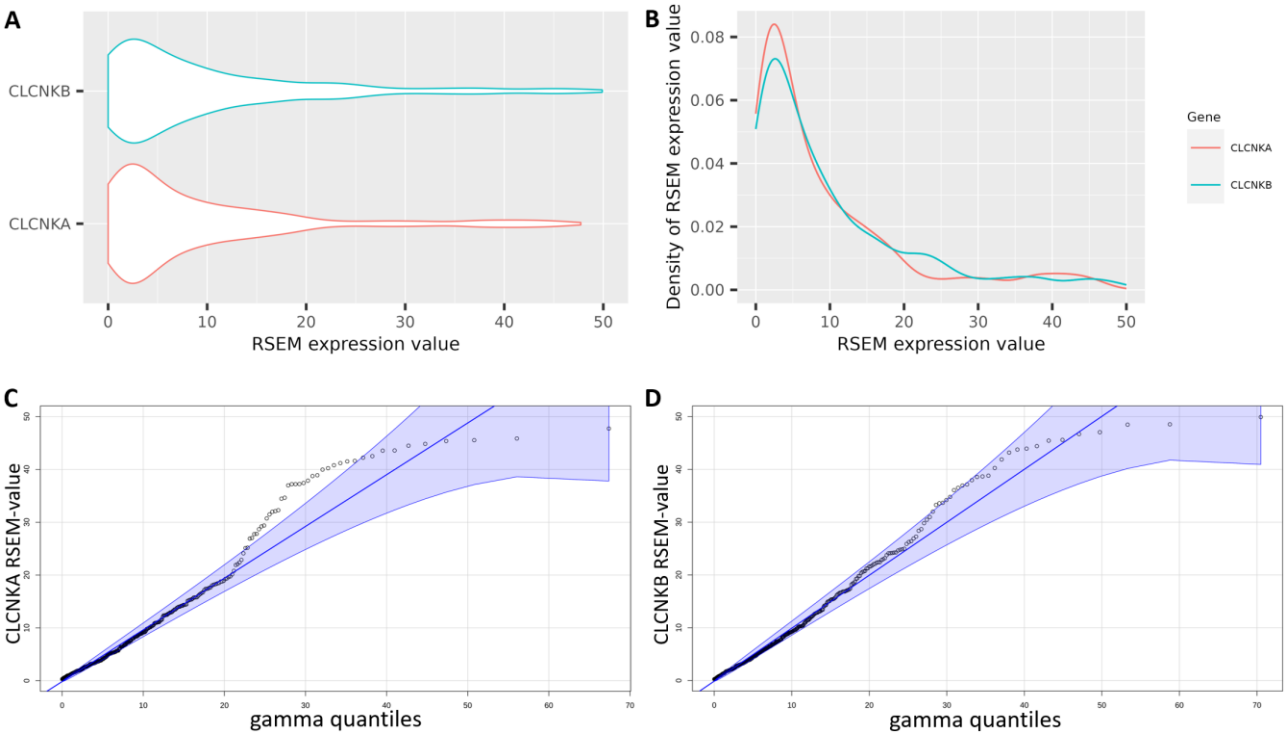
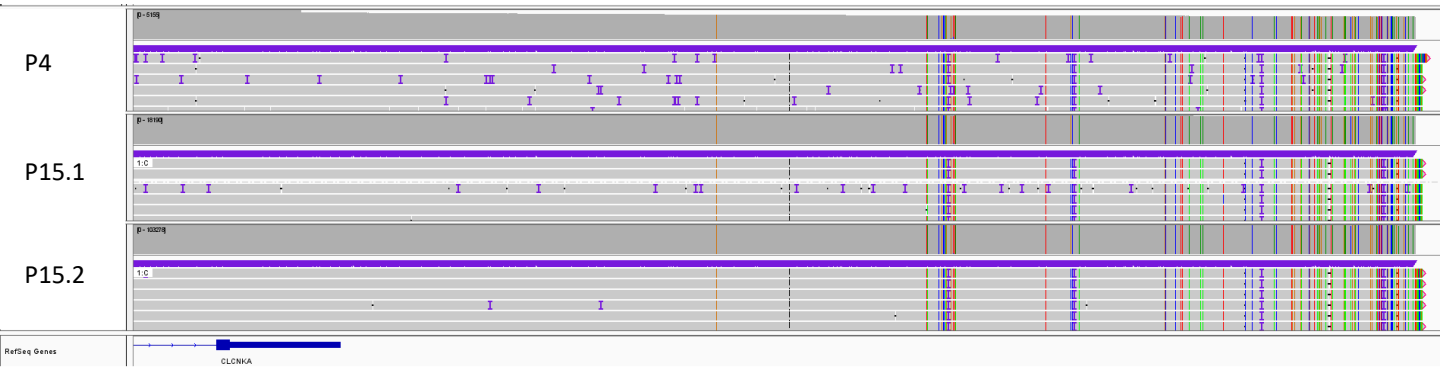


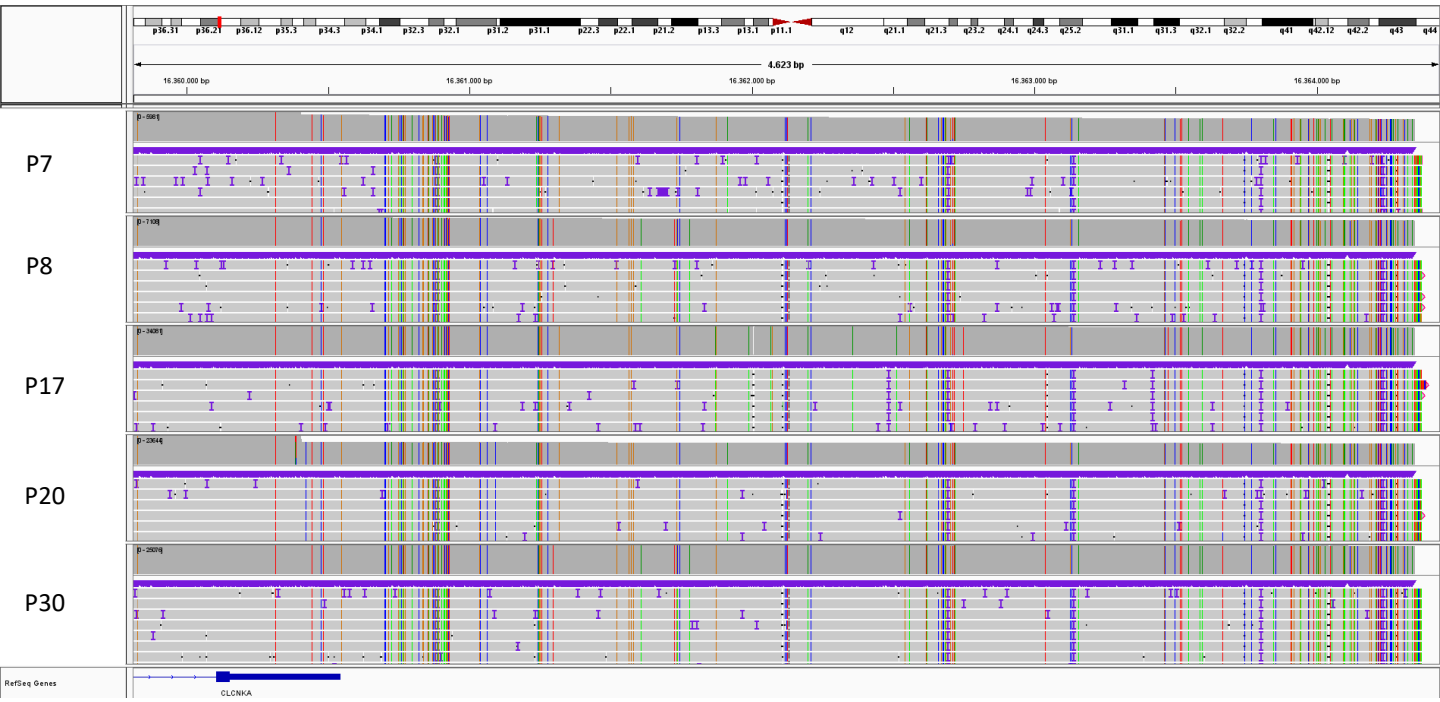
Fig. S5. Gene expression analysis for *CLCNKA* and *CLCNKB*

Gene expression analysis for *CLCNKA* and *CLCNKB* in renal clear cell carcinoma samples from the Pan-Cancer Atlas database (n=510). **A** Violin plot of expression levels in *CLCNKA* and *CLCNKB* between RSEM values of 0 and 50 (83.1% and 81.2% of observations for *CLCNKA* and *CLCNKB*, respectively). **B** RSEM expression value density plot for *CLCNKA* (red) and *CLCNKB* (blue) between RSEM values of 0 and 50. **C** Q-Q plot of *CLCNKA* RSEM expression values between 0 and 50 (zero values excluded) for the closest fit gamma distribution (p=0.0504). **D** Q-Q plot of *CLCNKB* RSEM expression between 0 and 50 (zero values excluded) for the closest fit gamma distribution (p=0.4076). The p-values for goodness-of-fit for a normal and lognormal distribution (Q-Q plots not shown) were all less than $1x10^{-5}$, hence the gene expression was deemed unlikely to correspond to these distribution categories.

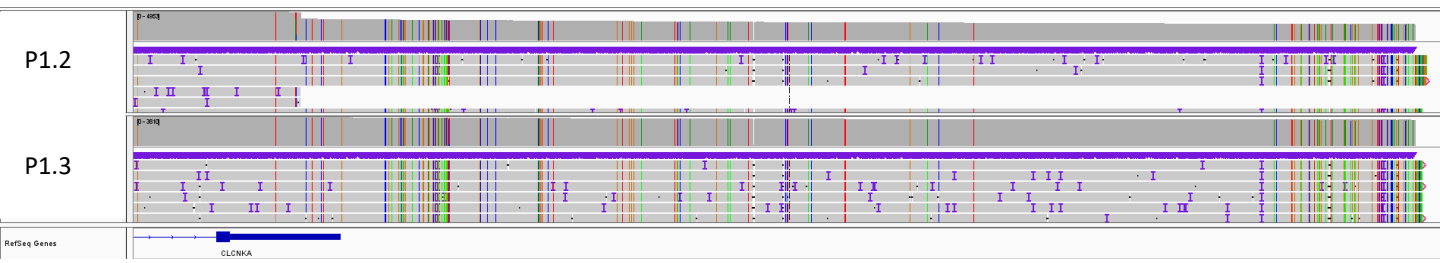
Deletion allele A



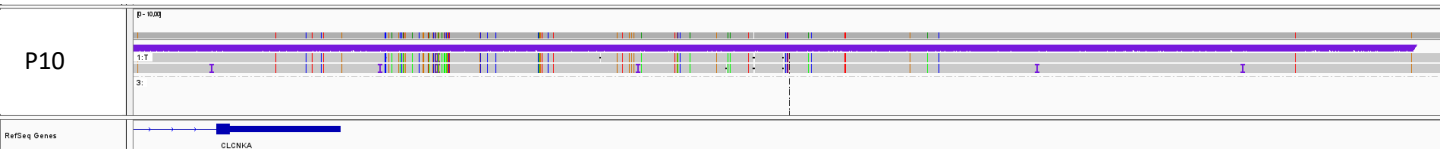
Deletion allele B



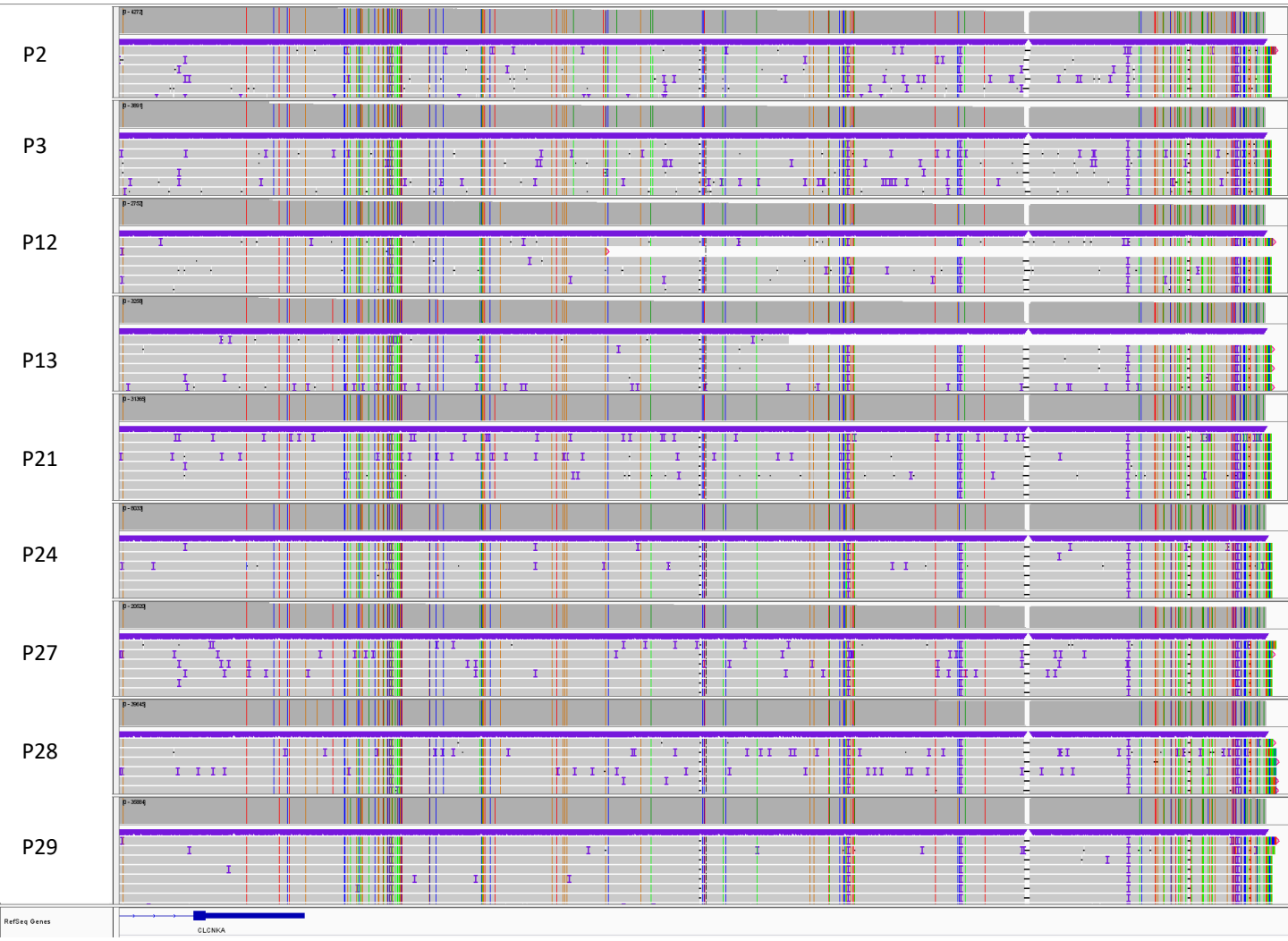
Deletion allele C



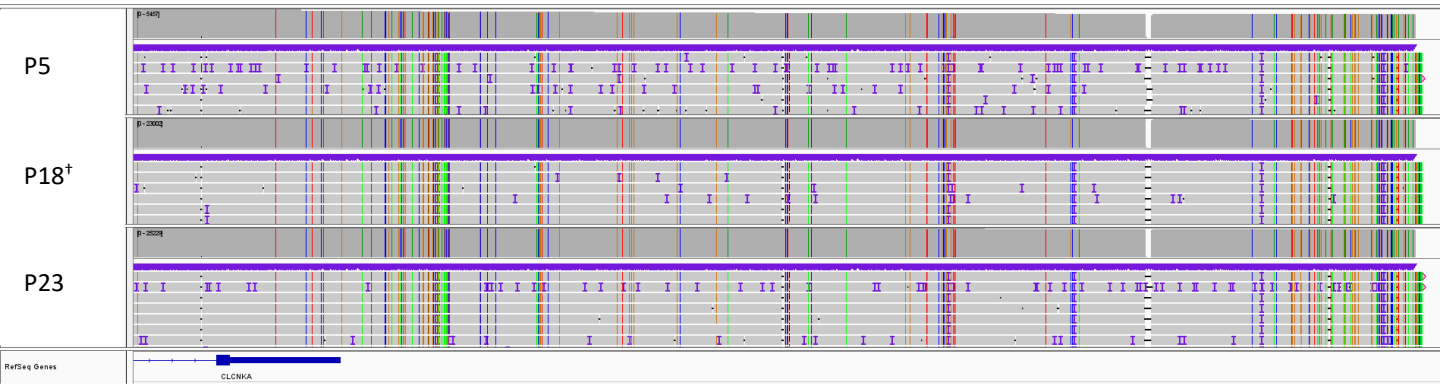
Deletion allele D



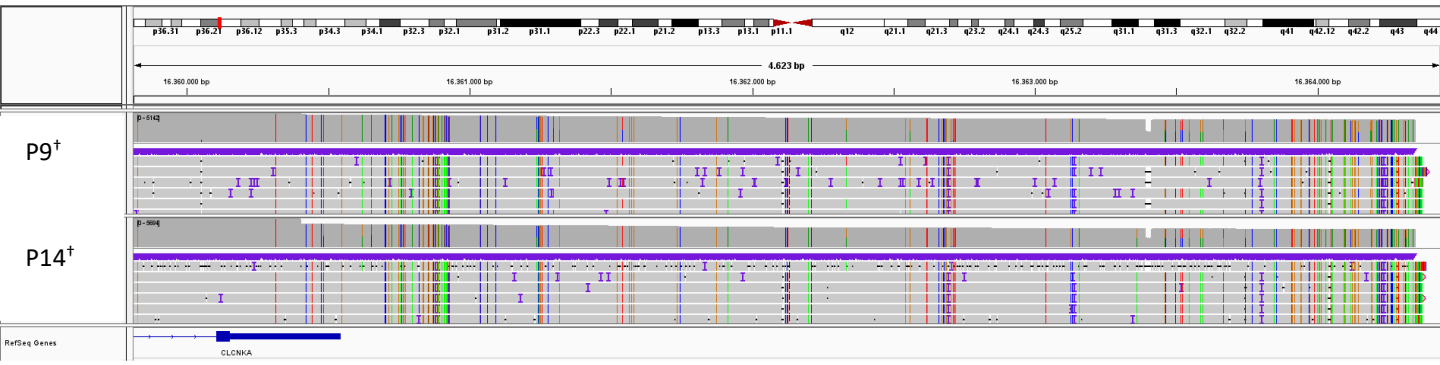
Deletion allele E



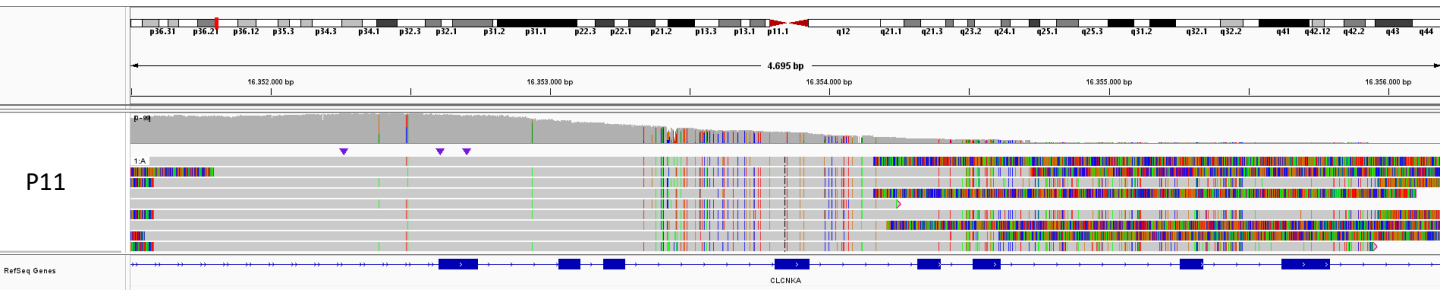
Deletion allele F



Deletion allele B + F



Deletion allele G



Deletion allele H

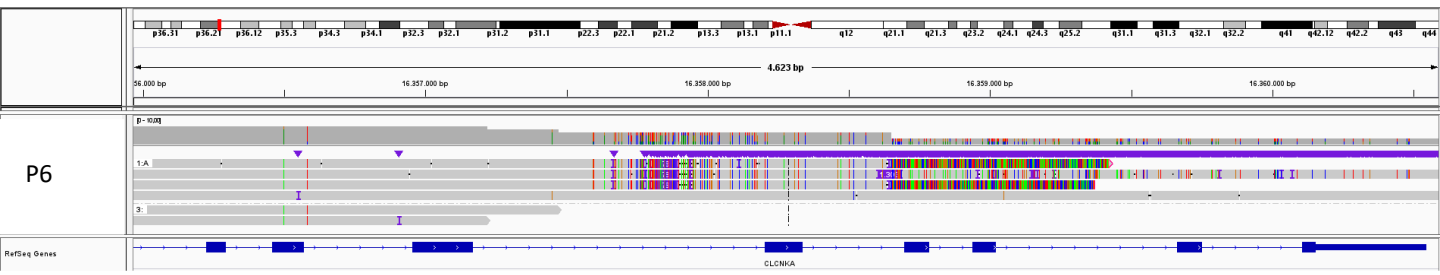


Fig. S6. Long-read Sequencing data.

Long-read Sequencing data of eight different deletion alleles (A-H) identified in 28 patients from this study visualized in IGV [26].