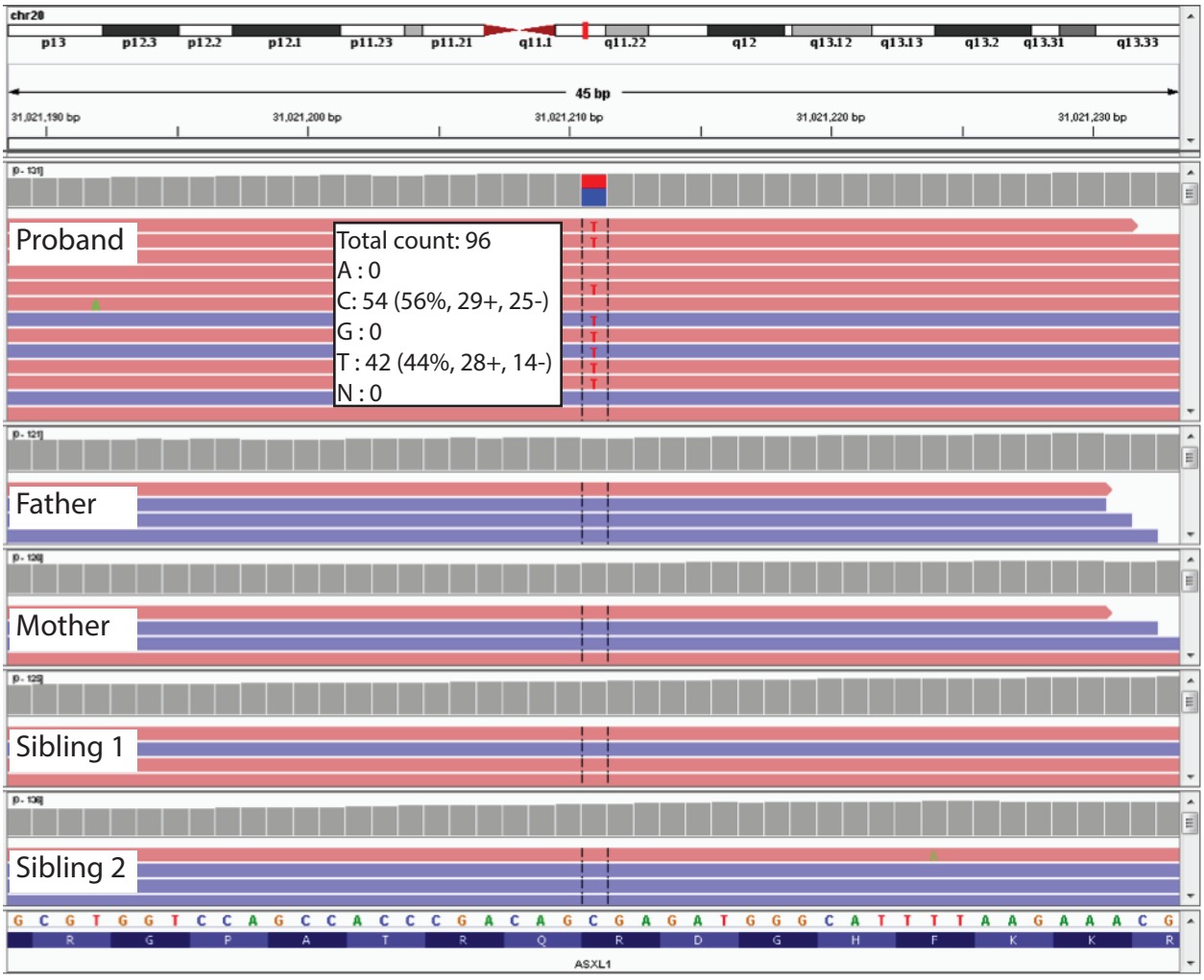
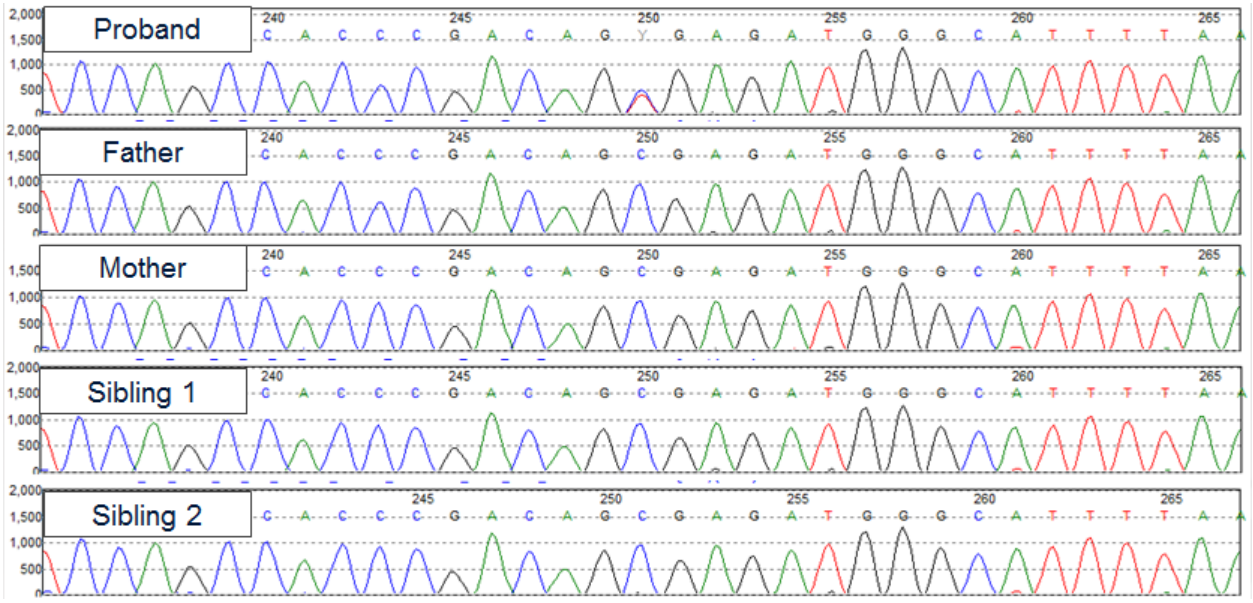
Supplementary Figure 1: *ASXL1 de novo* p.Arg404Ter variant. (A) IGV screenshot of the relevant region of *ASXL1* in proband, parents, and two unaffected siblings. Coverage was over 100 reads for each individual. (B) Sanger traces confirm the *ASXL1* p.Arg404Ter variant is present in the proband and not in unaffected family members (Mutation Surveyor v4.0.6). (C-D) UCSC Genome Browser screenshot of CRG Alignability track for 100 basepair reads and Duke Uniqueness track for 35 basepair reads shows good mappability for the *ASXL1* gene using the exon-only view with 50 basepair of adjacent sequence (C) and a 100 basepair window around the p.Arg404Ter variant (D) shows excellent mappability of reads for the *ASXL1* gene.

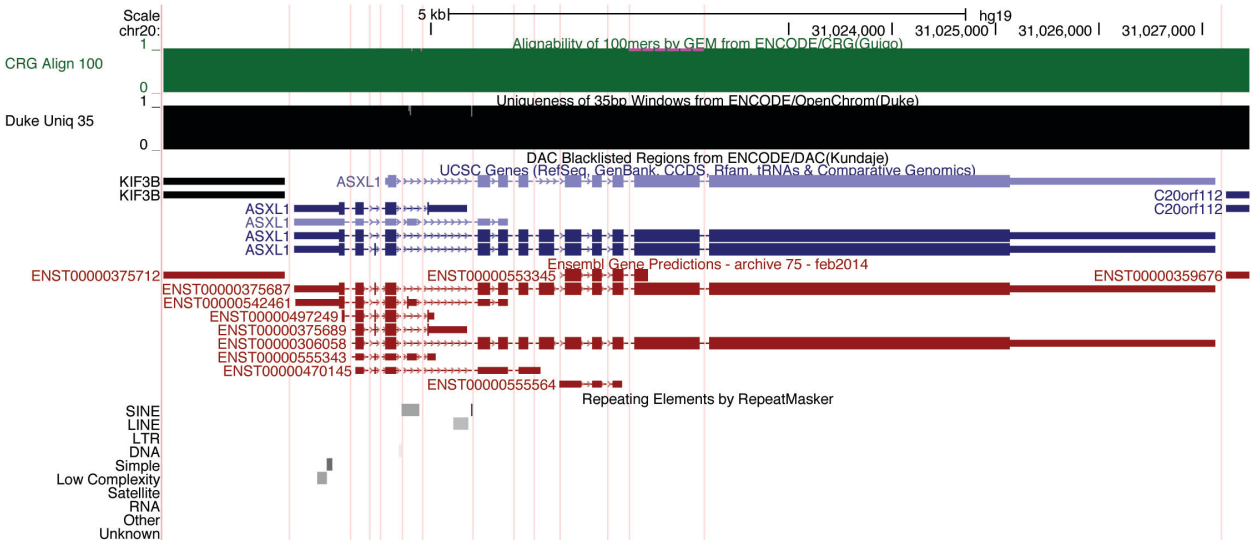
A. ASXL1 p.Arg404Ter (NGS – IGV)
chr 20: 31,021,211



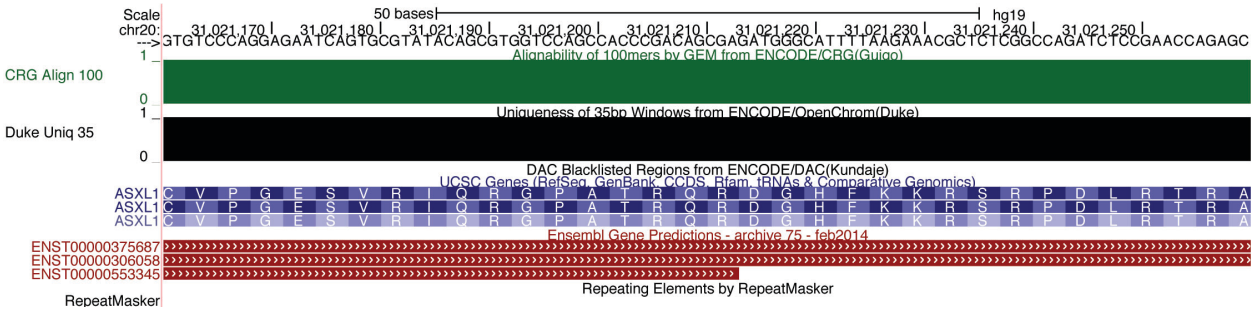
B. ASXL1 p.Arg404Ter (Sanger – Mutation Surveyor v4.0.6)
Chr 20:31021211



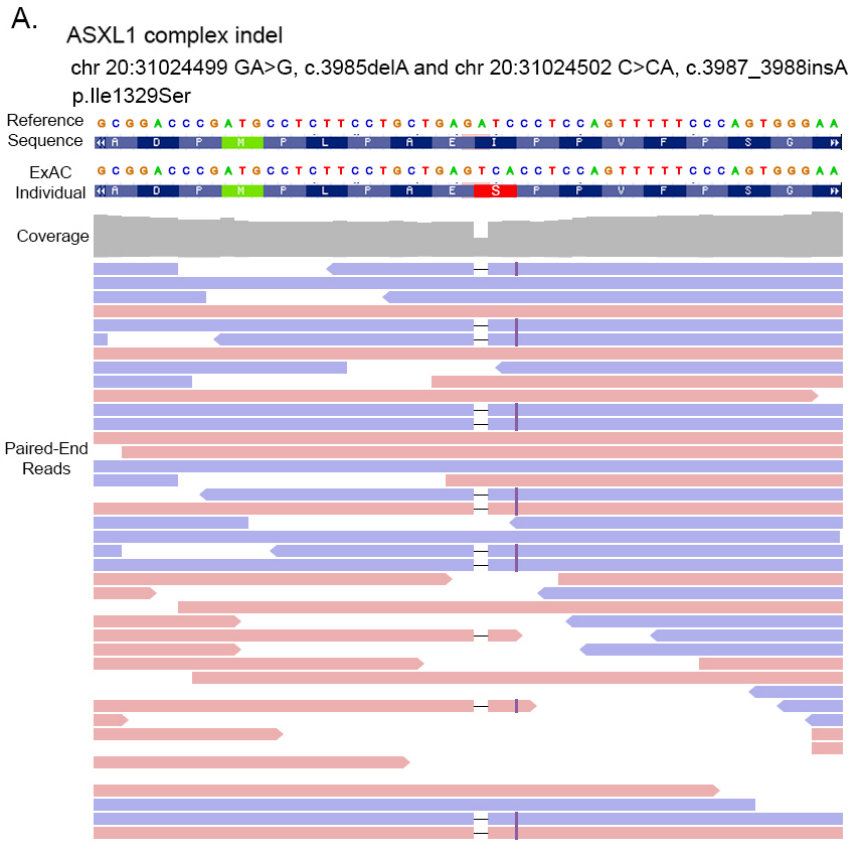
C.



D.

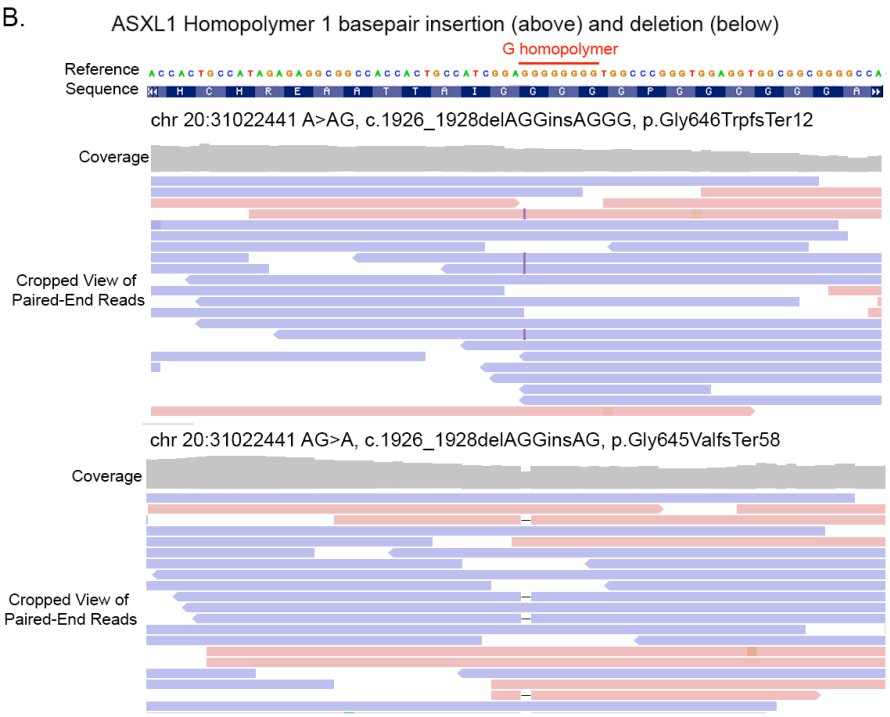


Supplementary Figure 2: Variants in *ASXL1* highlighted in the text. Blue and red reads indicate the direction of sequencing. (A) IGV screenshot of complex indel (1 basepair deletion and nearby insertion) that results in a missense substitution found in 2 individuals. (B) Representative IGV screenshot of insertion and deletion in G homopolymer region (reads cropped). (C) IGV screenshot of mosaic variant. Links to each variant on the ExAC browser are below the screenshots.



http://exac.broadinstitute.org/variant/20-31024499-GA-G

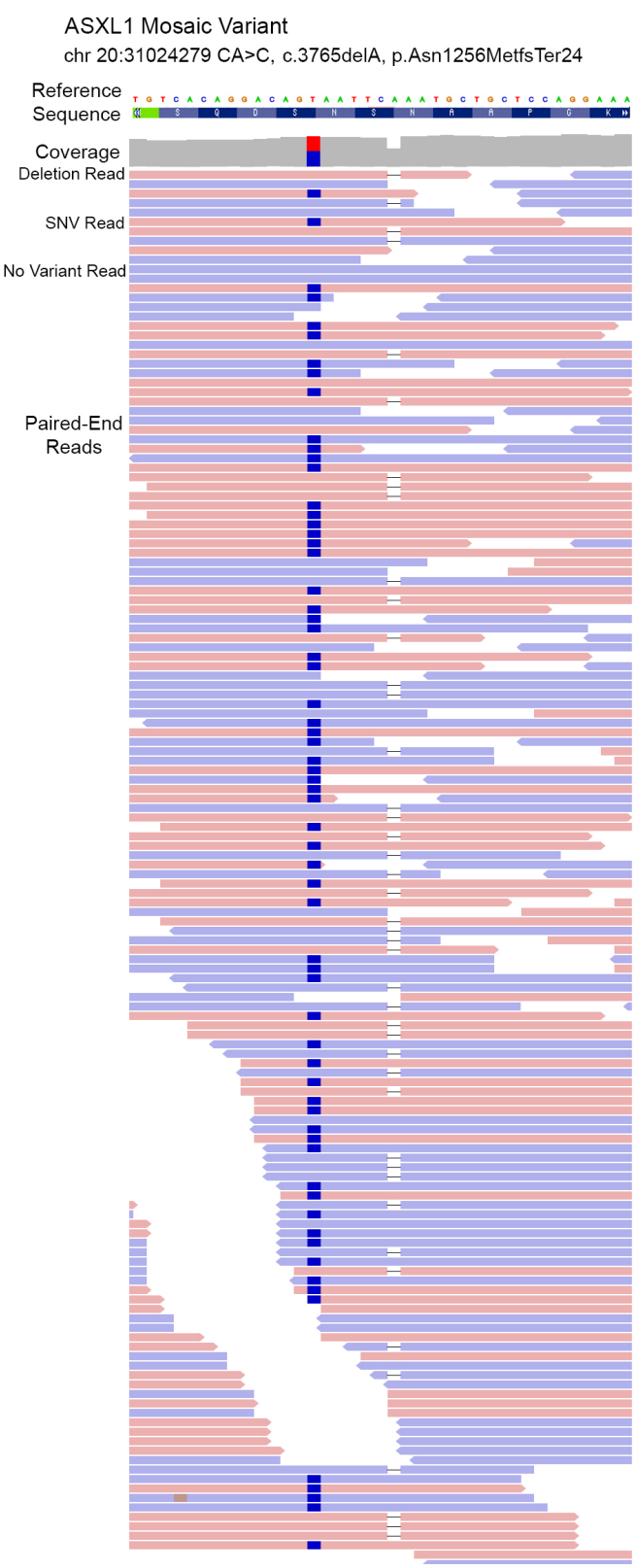
B.



http://exac.broadinstitute.org/variant/20-31022441-A-AG

http://exac.broadinstitute.org/variant/20-31022441-AG-A

C.



http://exac.broadinstitute.org/variant/20-31024279-CA-C