# Multiplex structural variant detection by whole-genome mapping and nanopore sequencing.

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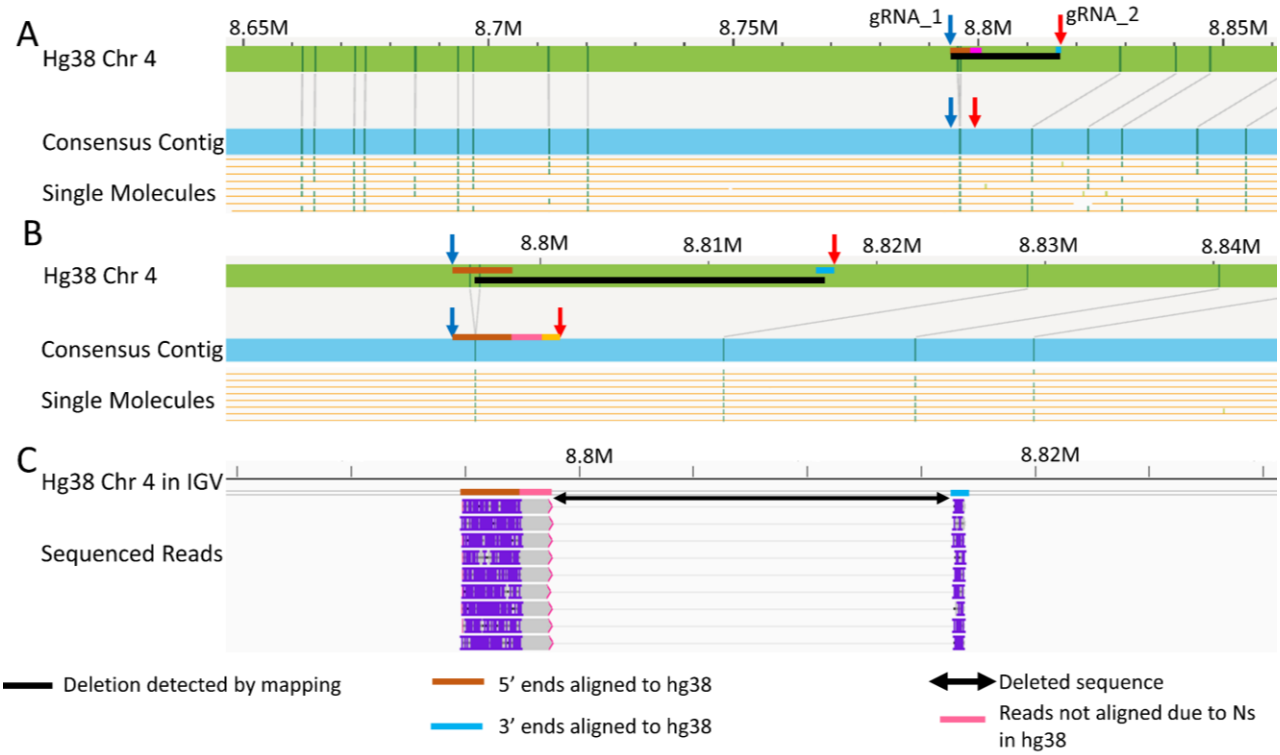


**Figure S1.** A homozygous deletion at chr4:8796117-8828957 resolved with our cas9-assisted targeted nanopore sequencing approach. Panel A shows optical map contigs of chromosome 4 between 8.65 and 8.85 Mbp. B shows a zoomed-in view of the maps around the deletion indicated by black bar. The blue and red arrows here represent the gRNAs designed to target the presumed deletion containing region. The three colored bars brown, pink and blue together represent the fragment generated by the gRNA pair. Panel C shows the sequenced reads aligning between the gRNA cut sites with a gap in between as expected. Coverage was 9X. The brown bar represents the part of fragments aligning on the 5'end and the blue bar represents the part of fragments aligning on the 3' end. The pink bar represents the part of fragments that do not align to hg38.

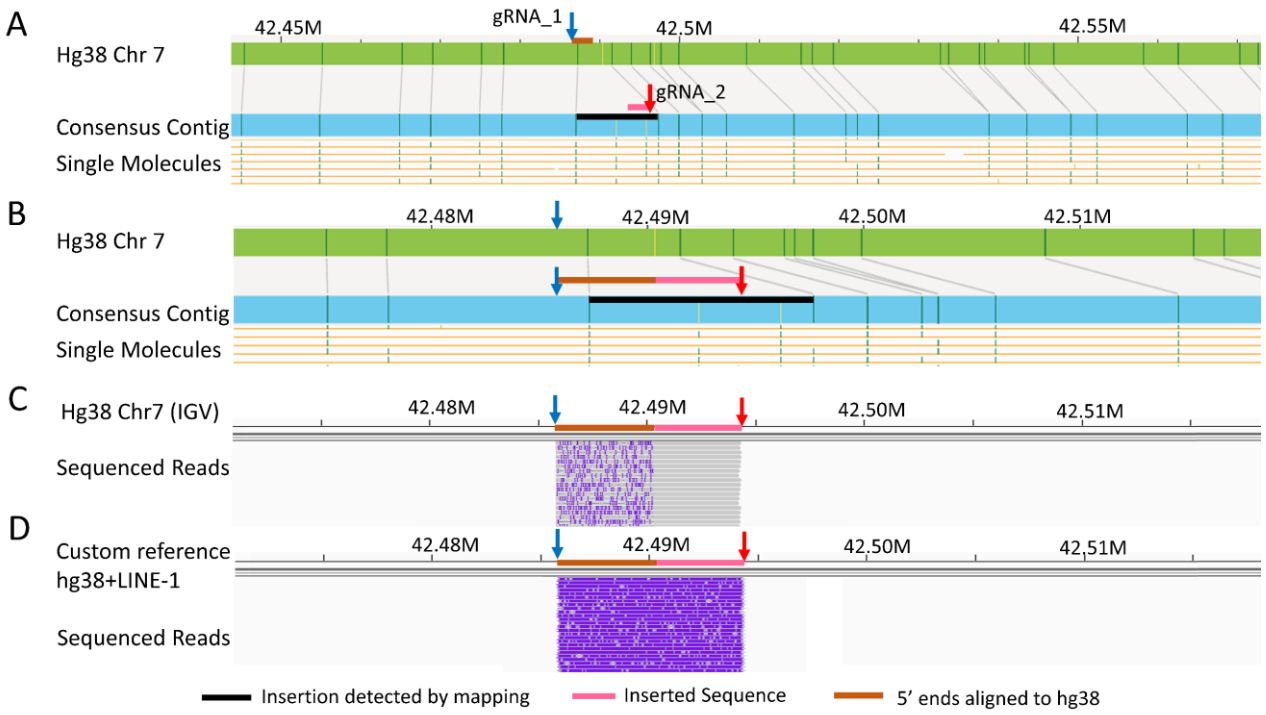


**Figure S2.** A LINE-1 insertion at chr7:42487230-42491515 resolved with our cas9-assisted targeted nanopore sequencing approach. Panel A shows optical map contigs of chromosome 7 between 42.45 and 42.55 Mbp. B shows a zoomed-in view of the maps around the insertion, indicated by black bar. The blue and red arrows here represent the gRNAs designed to target the presumed deletion containing region. The two, colored bars brown and pink together represent the fragment generated by the gRNA pair. Panel C shows the sequenced reads aligning between the gRNA cut sites expected. Coverage was 79X. The brown bar represents the part of fragments aligning on the 5'end and the blue bar represents the part of fragments aligning on the 3' end. The pink bar represents reads not aligning to hg38. Panel D shows the same reads aligning to a custom reference where the reference consisted of hg38 sequence with a LINE-1 reference inserted at the detected breakpoint.

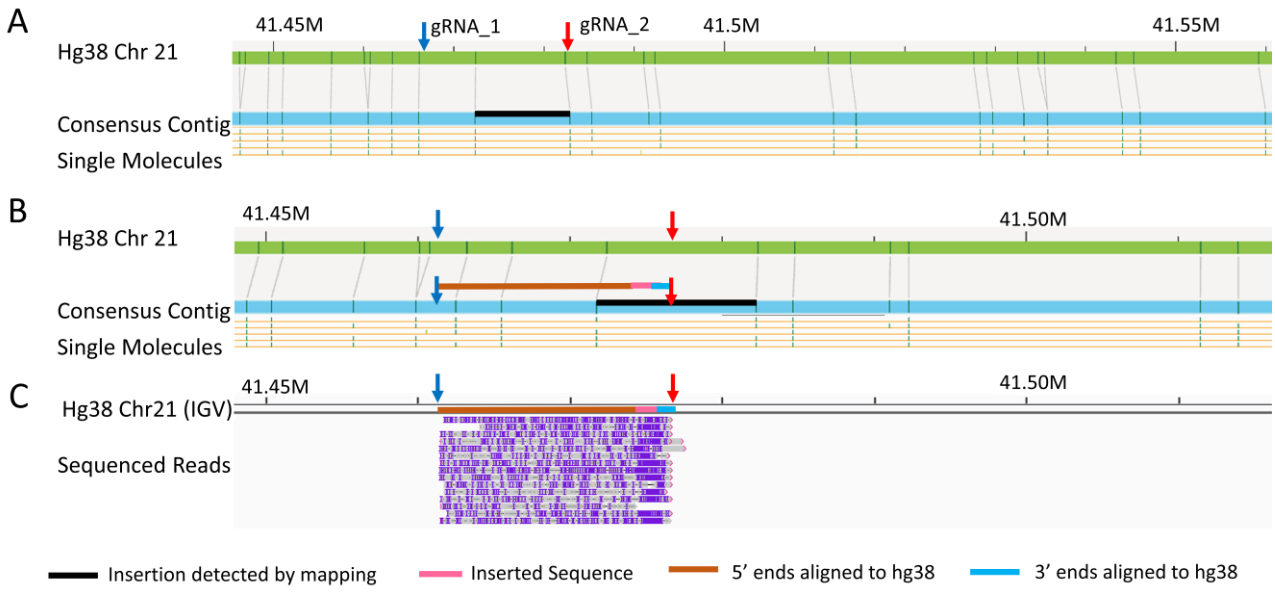


**Figure S3.** A homozygous insertion at chr21:41454955-41484741 resolved with our cas9-assisted targeted nanopore sequencing approach. Panel A shows optical map contigs of chromosome 21 between 41.45 and 41.55 Mbp. B shows a zoomed-in view of the maps around the insertion indicated by black bar. The blue and red arrows here represent the gRNAs designed to target the insertion containing and its flanking regions. The three colored bars brown, pink and blue together represent the fragment generated by the gRNA pair. Panel C shows the sequenced reads aligning between the expected gRNA cut sites with an insertion marked. Coverage was 14X. The brown bar represents the part of fragments aligning on the 5'end and the blue bar represents the part of fragments aligning on the 3' end. The pink bar represents the part of fragments that do not align to hg38.

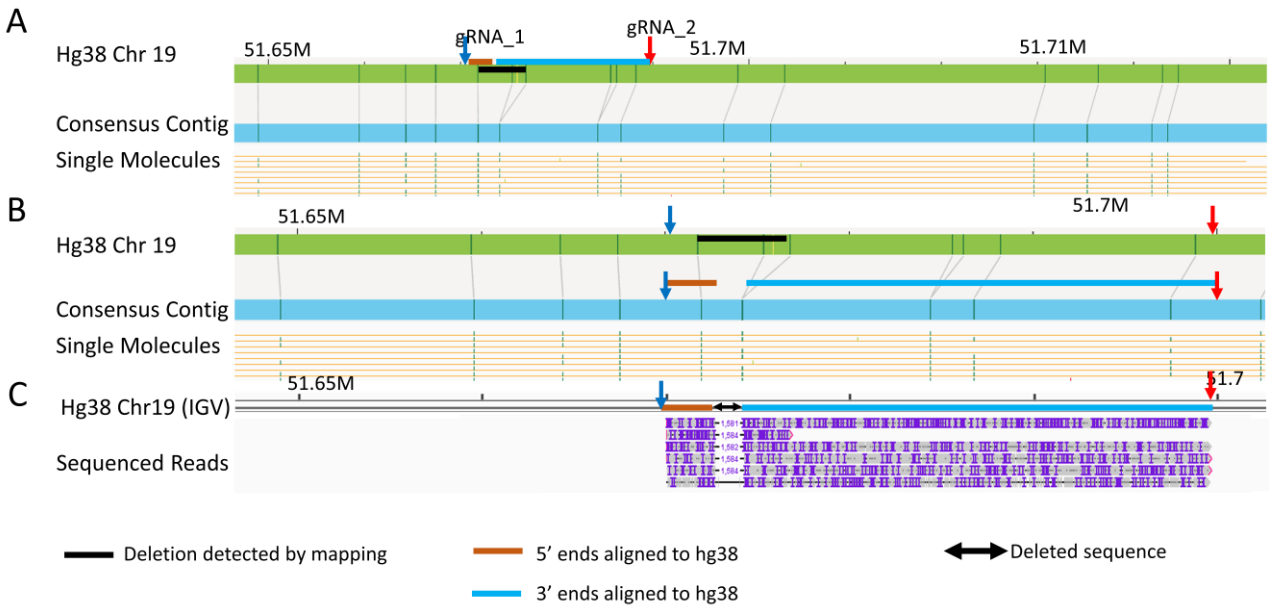


**Figure S4.** A deletion at chr19:51651518-51757499 resolved with our cas9-assisted targeted nanopore sequencing approach. Panel A shows optical map contigs of chromosome 4 between 51.65 and 51.72 Mbp. B shows a zoomed-in view of the maps around the deletion indicated by black bar. The blue and red arrows here represent the gRNAs designed to target the presumed deletion containing region. The two, colored bars brown and blue together represent the fragment generated by the gRNA pair. Panel C shows the sequenced reads aligning between the gRNA cut sites with a gap in between as expected. Coverage was 6X. The brown bar represents the part of fragments aligning on the 5'end and the blue bar represents the part of fragments aligning on the 3' end.

**Table S1: List of target SVs designed gRNAs and detected breakpoints.**

| SV Genomic Region | gRNA_1 | gRNA_2 | gRNA_3 | SV | Detected breakpoints (bp) |
|---|---|---|---|---|---|
| chr4:8796117-8828957 | GGGGGACTCTGAACACAAGT | GGATACGTCACCTCTTTGAA | | Deletion | 8797478 |
| chr12:45504427-45517614 | TTGCACCACAACTTGTCAGA | CACATTGAGAACCTCTGCTA | GTCCAAGAGTAAGCACCCCA | Deletion | 45509371 |
| chr19:8282857-8293646 | GTCCCAATCTGGACTCCTAG | CATCGACTGCCCAAGCCAAG | | Deletion* | 8277069 |
| chr1:152555548-152587768 | ACTGACACCTCTATAGATAC | CTATTTGCATTGACCACTGC | ACTTTTCTTGGATGATACCG | Deletion | 152583066 |
| chr6:167590126-167652737 | CATCTGGTCTGGTCACCTAC | AAGCCAAGGTATACCCATGC | GGTCGAATTCCGGAGACACT | Deletion | 167591394 |
| chr3:186650273-186655454 | TTGACCCAAGGGTAGAACTA | AGGAAGATCTACCAAGCCAA | | Insertion** | 186654352 |
| chr7:42487230-42491515 | GATGAATTCGATTTCTGTGT | AGGAAGATCTACCAAGCCAA | | Insertion** | 42490277 |
| chr6:13500995-13504649 | AGGAAGATCTACCAAGCCAA | AAGGATACTAAAATACCCAC | | Insertion** | 13502803 |
| chr1:48958322-48966134 | TAGCCTTTAGCATCACACTC | AGGAAGATCTACCAAGCCAA | | Insertion** | 48963085 |
| chr12:33854180-33867084 | AAGTTCTTTATCTGTTTGTT | AGGAAGATCTACCAAGCCAA | | Insertion** | 33864403 |
| chr12:17649268-17936894 | GGGACATTACGTCAACCTAA | ATAGGAGTTTACCCAGTCCT | | Inversion | 17768358, 17861570 |
| chr21:41454955-41484741 | TGAGGCAGGAAAATCGAGTC | GCCCTGGCAGCCACCTAACG | | Insertion | 41474066 |
| chr3:10121283-10167205 | CAGGAGTTTAAGACCAGCCT | CCAGGAGTTAAAACCAGCCT | | Insertion | 10134067, 10134166 |
| chr19:51651518-51757499 | GATCACCTGAGGTCAGGAGT | TTGCCCAGGCTGGCGTACAG | | Deletion | 51672676, 51674261 |

* We estimate the deletion size to be ~15 kbp and that secondary alignment is due to sequence similarities in the flanking regions.
** LINE-1 Insertion