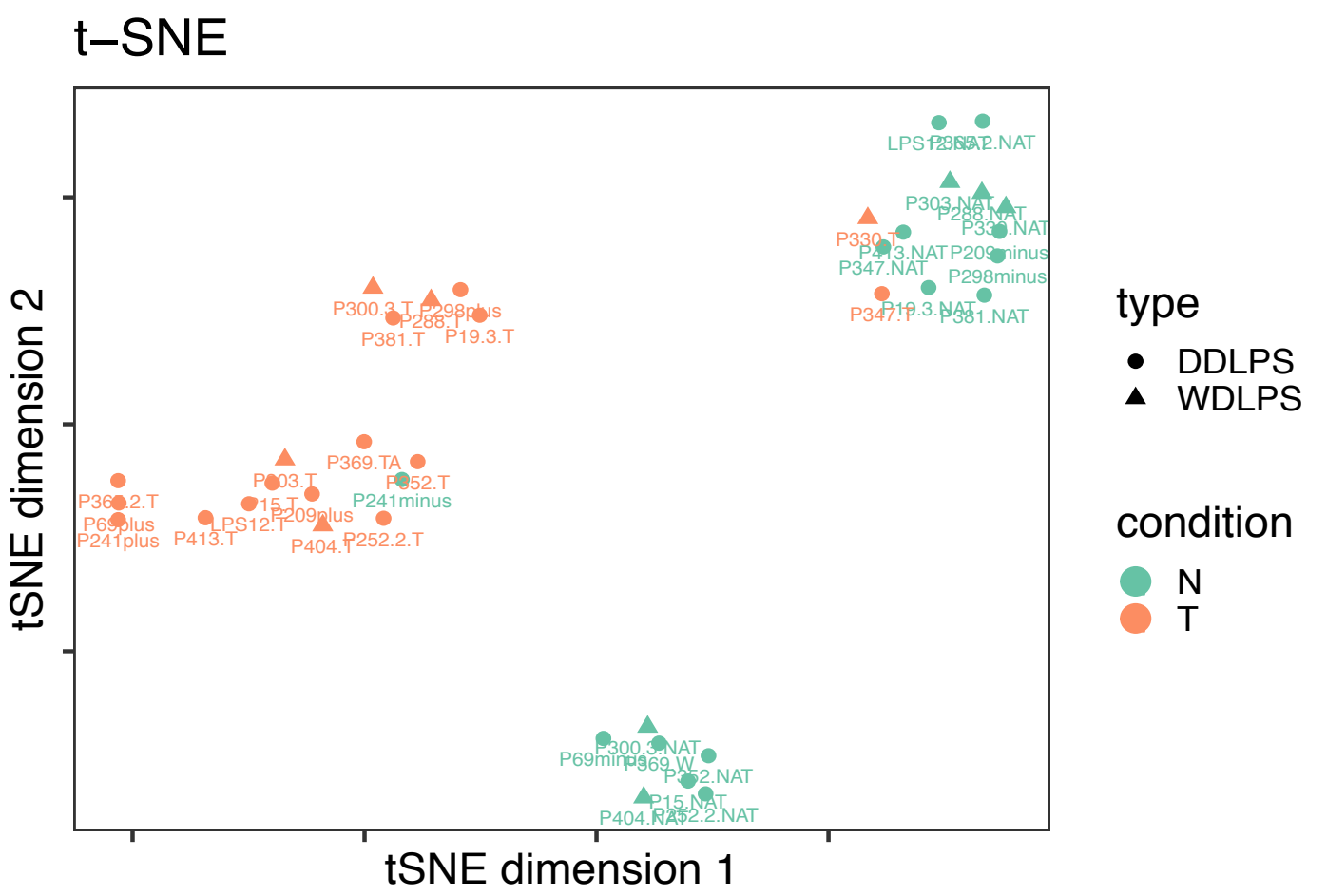
a



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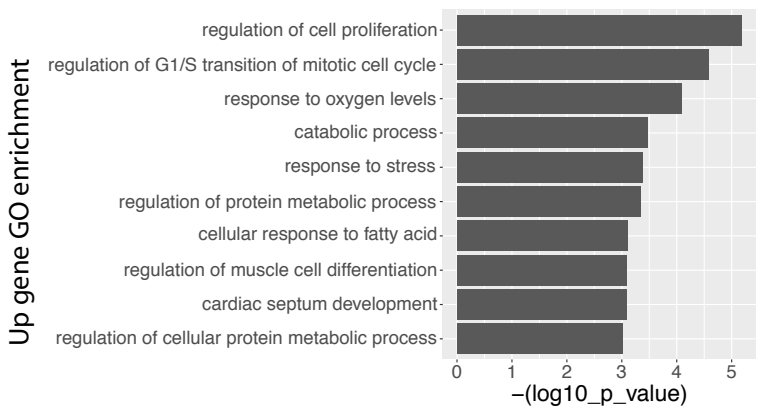
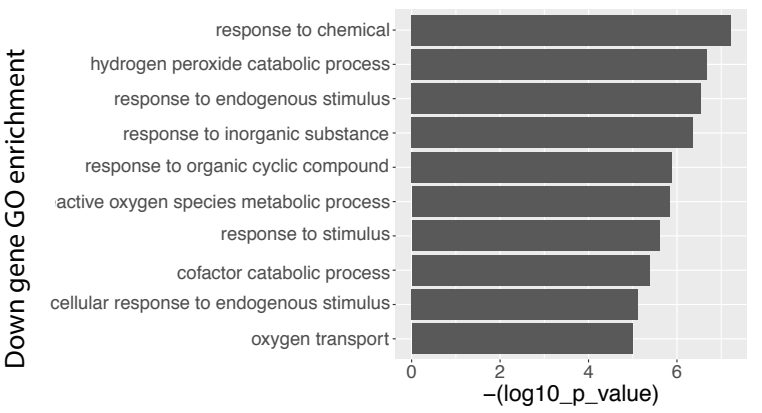
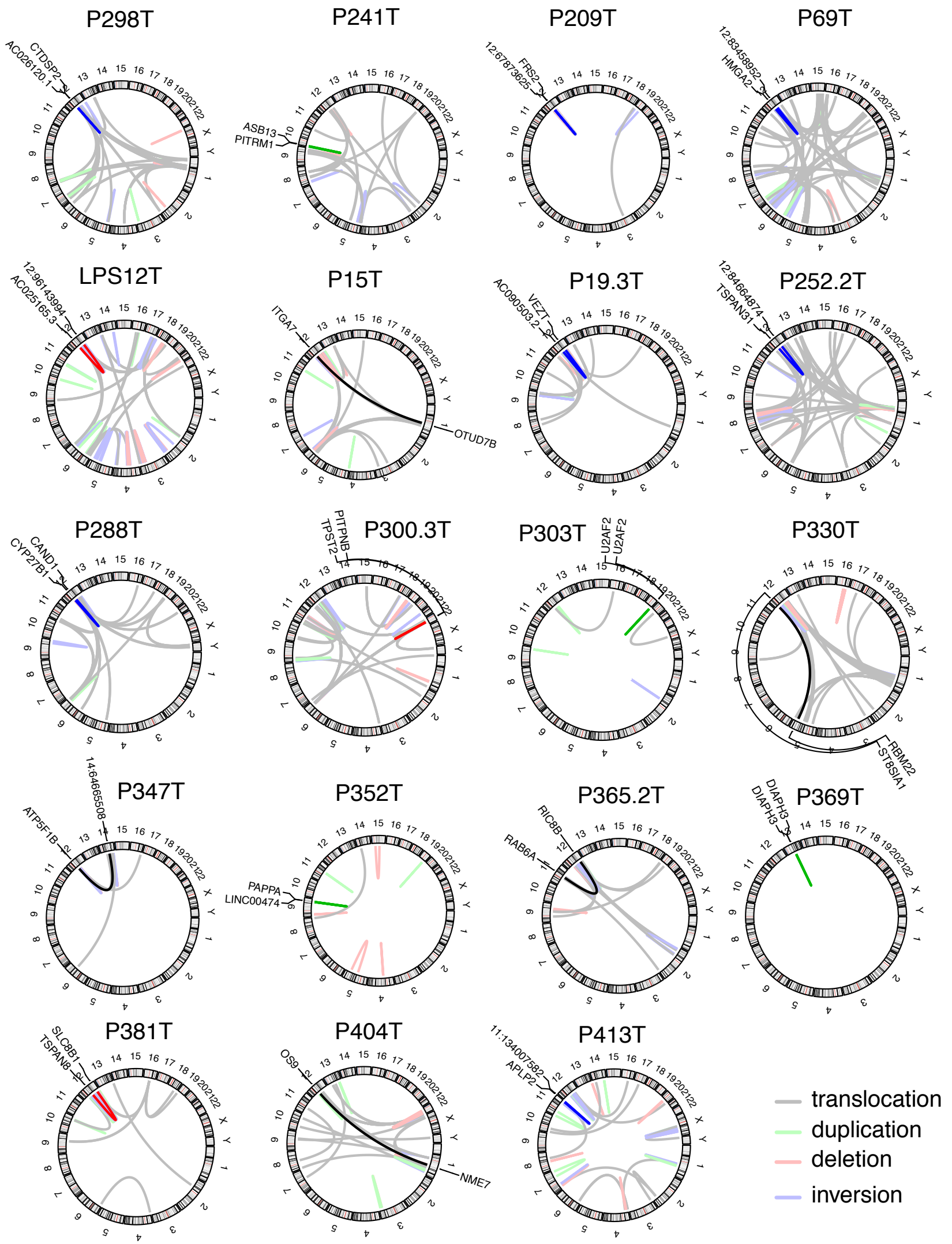


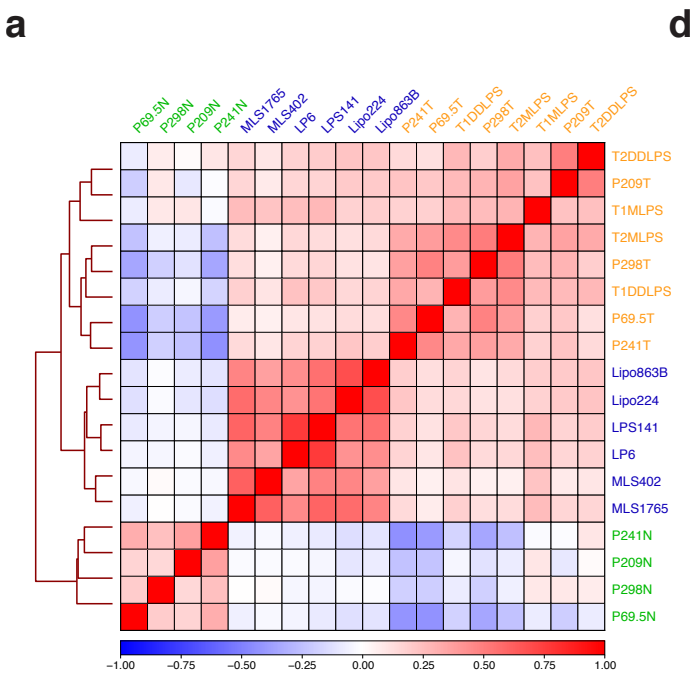


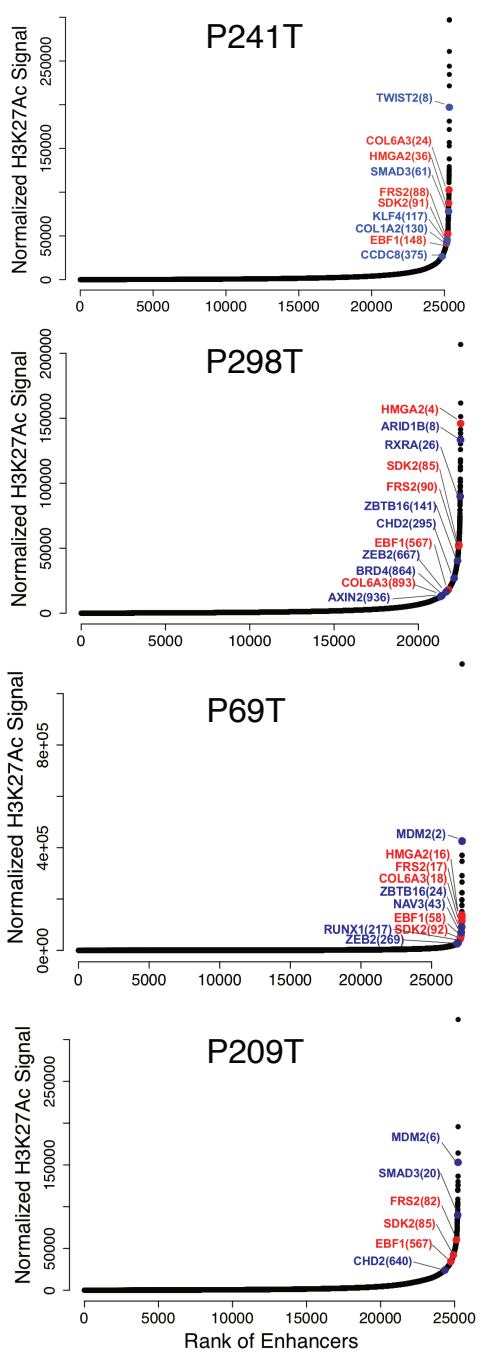
Supplementary Figure 1. Patient sample classification. a. t-SNE plot showing the classification of patients based on the top 500 most variable genes. **b**. Go term enrichment analysis for up/down-regulated genes from Figure 1b.

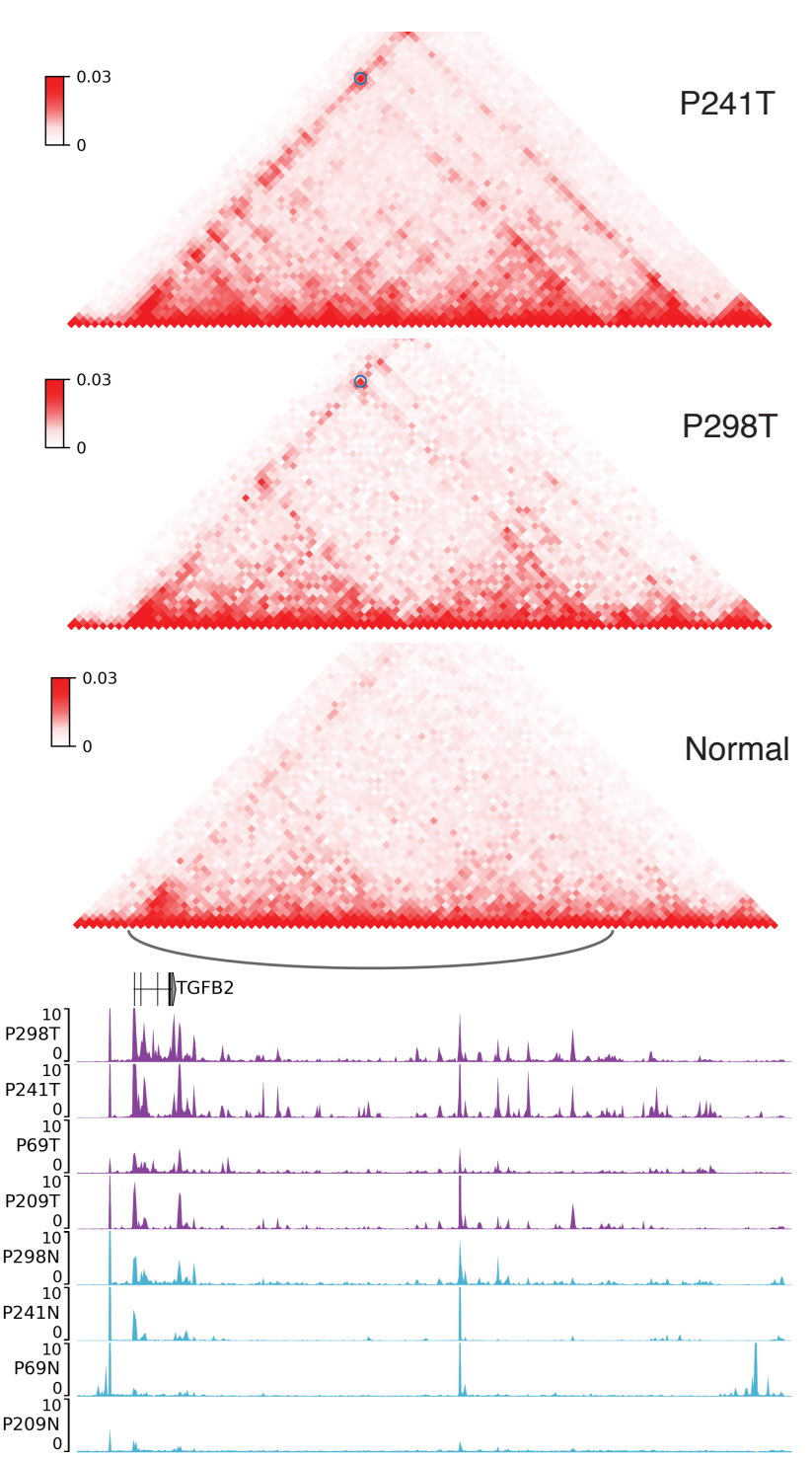
a



Supplementary Figure 2. Gene fusion events identified in the 19 patient tumor samples. a. Circos plot to show the fusion gene events in each patient tumor sample. The top confident fusion gene in the sample was annotated and highlighted.

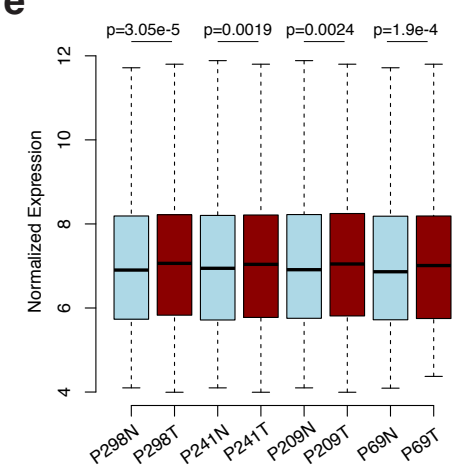




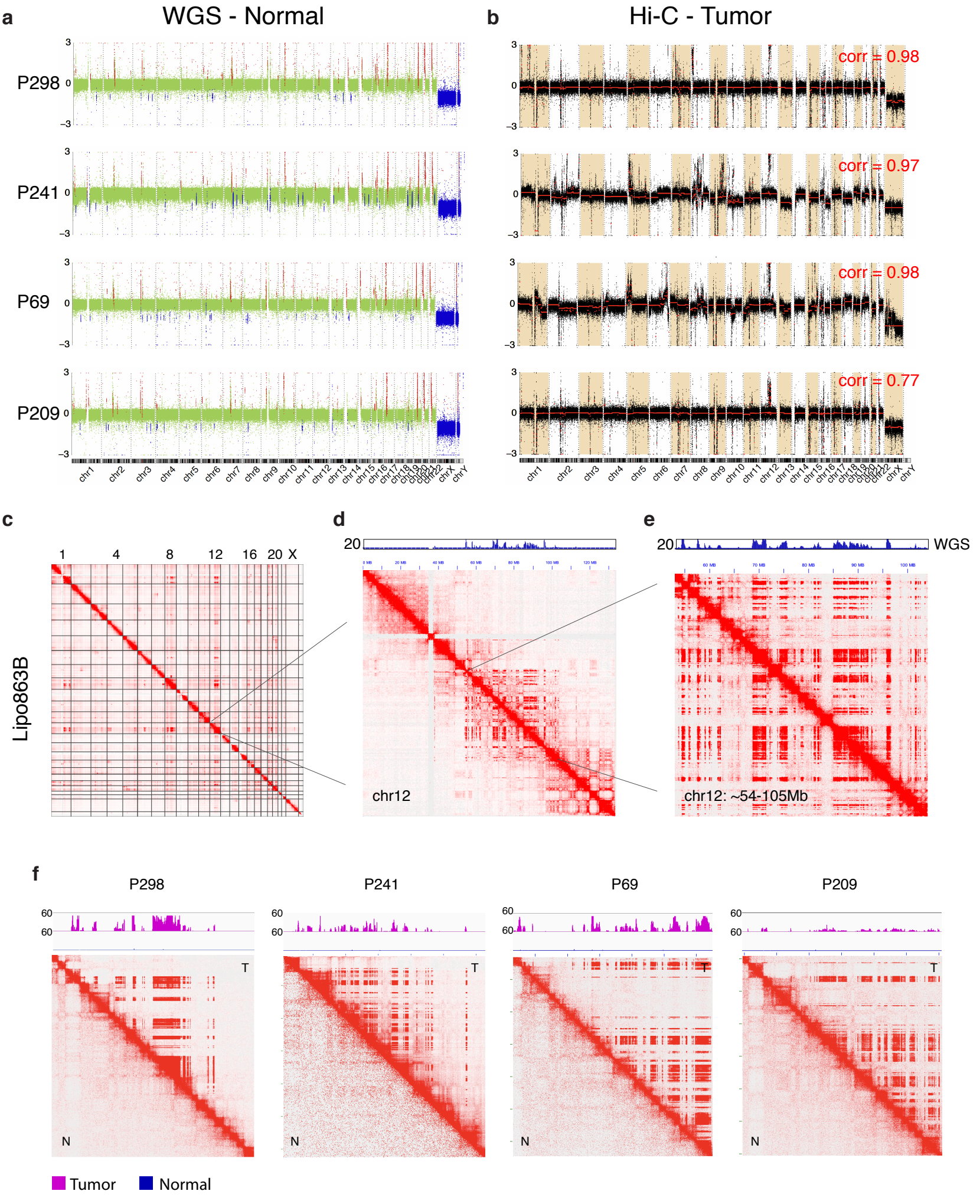


c

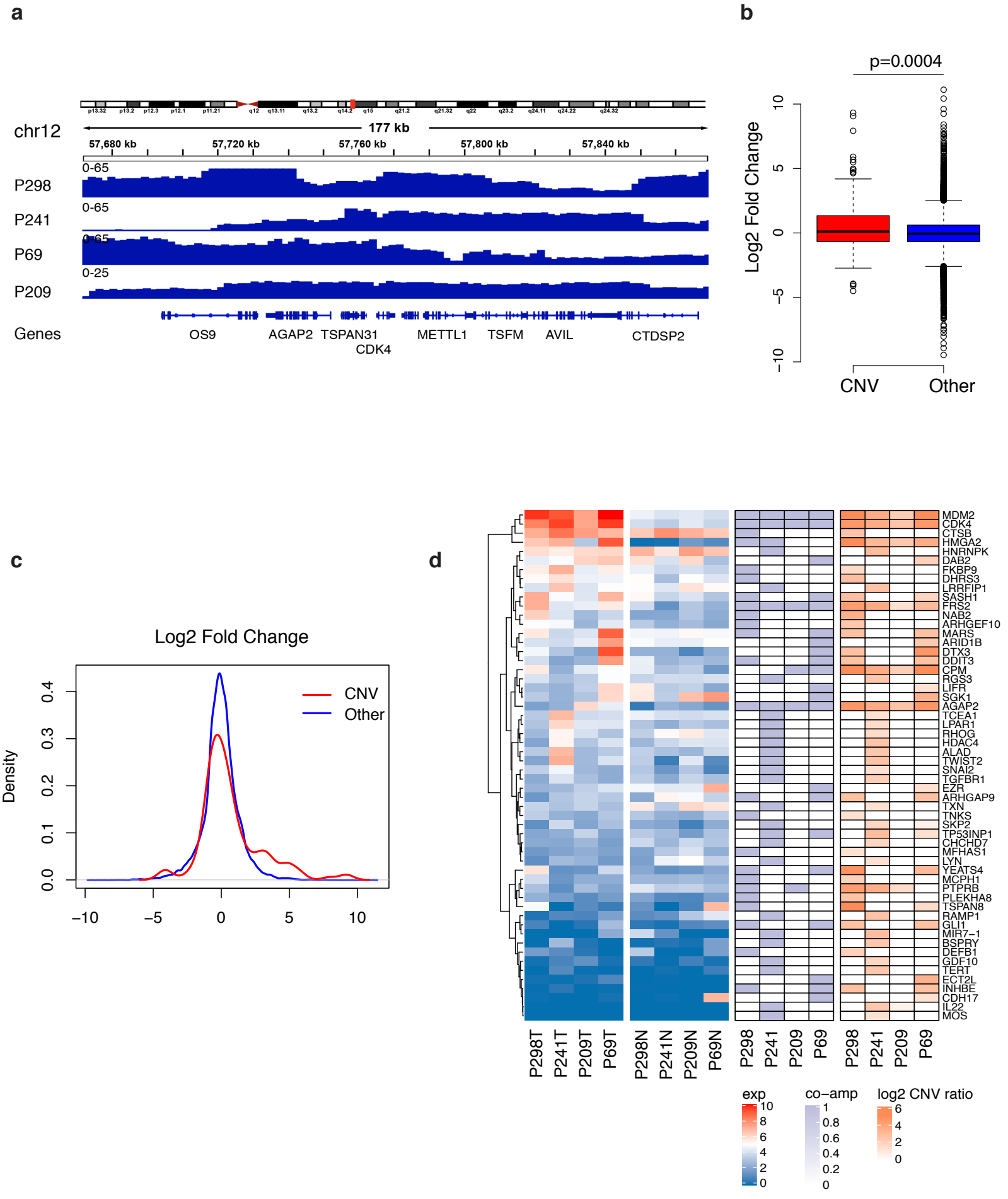
Seq Logo	Motif	Enrichment of motifs in tumor specific gain of enhancers	Enrichment of motifs in tumor specific loss of enhancers
	JUND(var2)	1e-34	NA
	ATF7/ATF2	1e-23	NA
	ATF1	1e-17	NA
	Arid3a	1e-14	1e-1
	TWIST1	1e-12	NA
	NFIX	1e-12	NA
	c-Jun-CRE	1e-20	NA
	AP-1	1e-11	NA
	E2F1	1e-9	NA



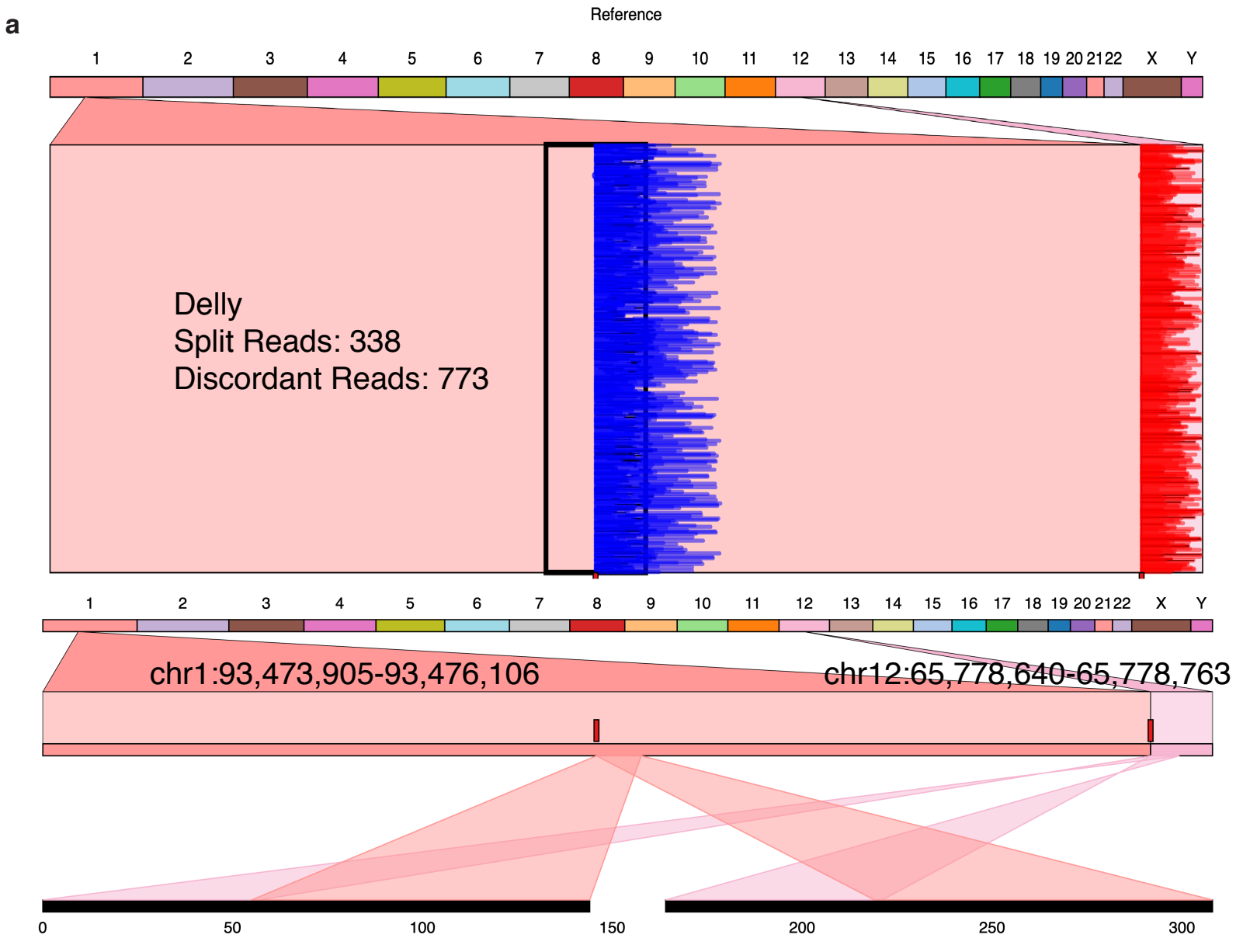
Supplementary Figure 3. Enhancer and chromatin interaction landscape in Liposarcoma patient samples. **a**. Hierarchical clustering H3K27Ac profile based on the sample correlations. The samples are color coded into brown (patient samples), blue (cell lines) and green (patient normal samples). **b**. The super-enhancer related genes identified in each patient tumor tissues. Genes in red are recurrent in at least two of the samples. **c**. Motifs enriched at tumor specific enhancers. **d.** Cancer specific chromatin interactions involving TGFB2 genomic region. The blue circles on the Hi-C map highlights the positions of the cancer specific interactions as well as the arcs below the Hi-C maps. The top two panels of the Hi-C maps are from the P241, and P298 patient tumor samples and the bottom panel shows the merged Hi-C matrix from all the normal tissue samples. The tracks below are the H3K27Ac ChIP-seq profiles for the patient samples from both tumor (purple) and normal (blue) tissues. **e**. Boxplot for normalized expression of cancer-specific chromatin interaction involved genes.

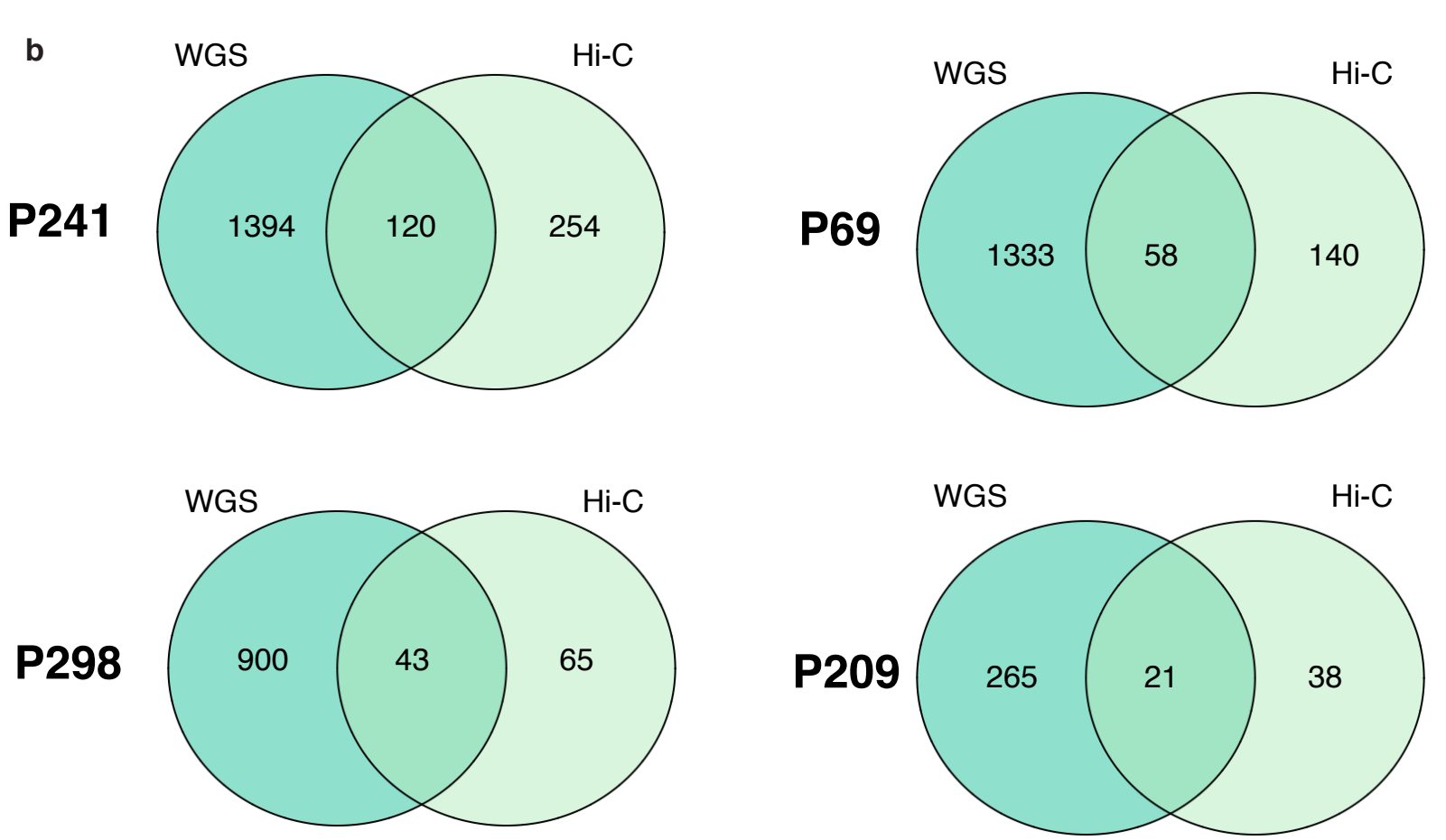


Supplementary Figure 4. The copy number variations identified from Hi-C and WGS dataset. a. The CNV profiles for P298, P241, P69 and P209 normal samples identified from WGS data. **b.** the CNV profiles for P298, P241, P69 and P209 tumor samples inferred from Hi-C data. The Pearson correlation between CNV profiles inferred from Hi-C and WGS are showed on each profile. **c**. The genome-wide Hi-C map for Lipo863B. **d**. The zoom-in Hi-C map for chr12. **e**. The zoom-in Hi-C map for chr12:54-105Mb region. **f**. the Hi-C map for chr12:60-80Mb in the 4 patient samples, the two top panels are the corresponding WGS tracks (purple: tumor, blue: normal).

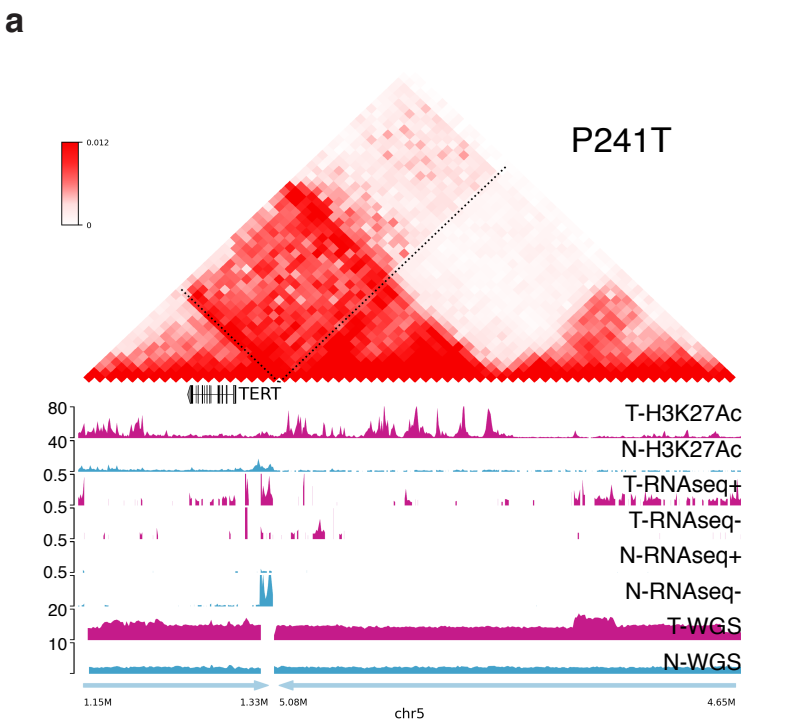


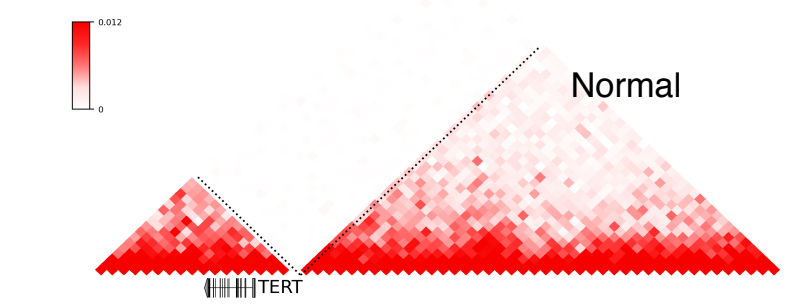
Supplementary Figure 5. Enhancer co-amplification for oncogenes. **a**. The WGS tracks on a recurrently amplified region on chr12. **b**. Boxplot for log2FC of the 138 copy number gain genes and the rest of the gene. **c.** Density plot of 138 gene with copy number gain (red) and the rest of the genes (blue). **d**. The expression profile for the oncogenes with enhancer co-amplification from at least one patient sample.

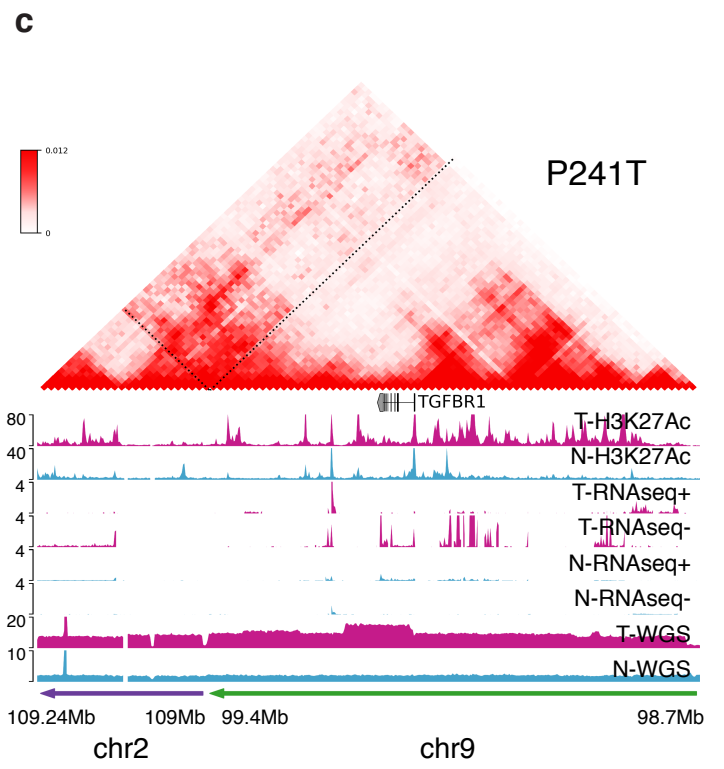


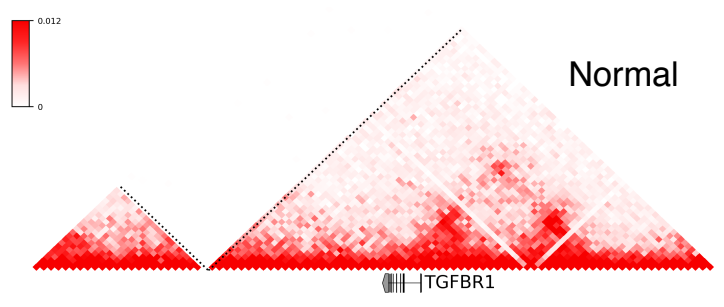


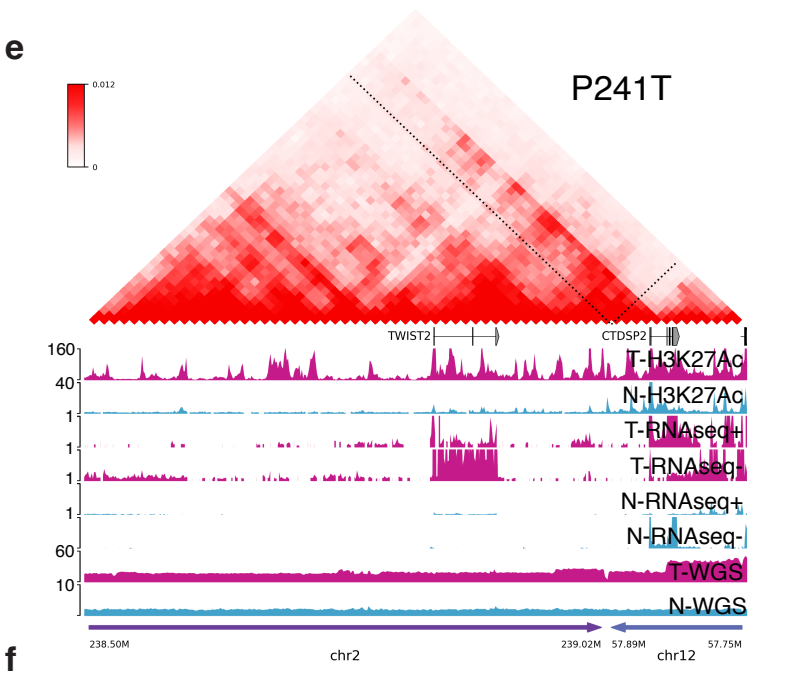
Supplementary Figure 6. Structure variations in LPS. a. The reads alignment figure generated from Ribbon showed one example of the translocation event identified from WGS data. The breakpoint is also consistently identified from Hi-C data. **b**. Venn Diagram showed the number of structure events identified from WGS or Hi-C or both in each patient sample.

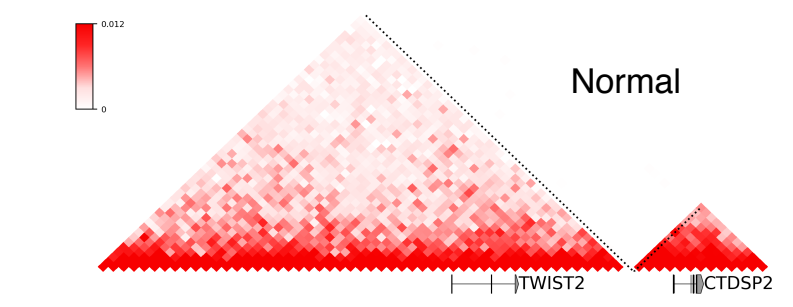


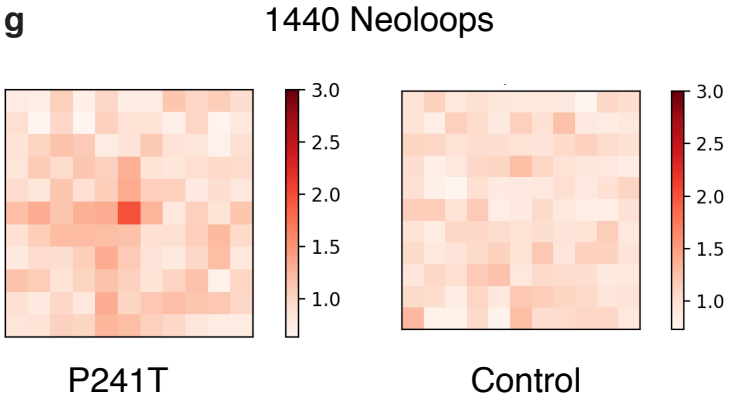


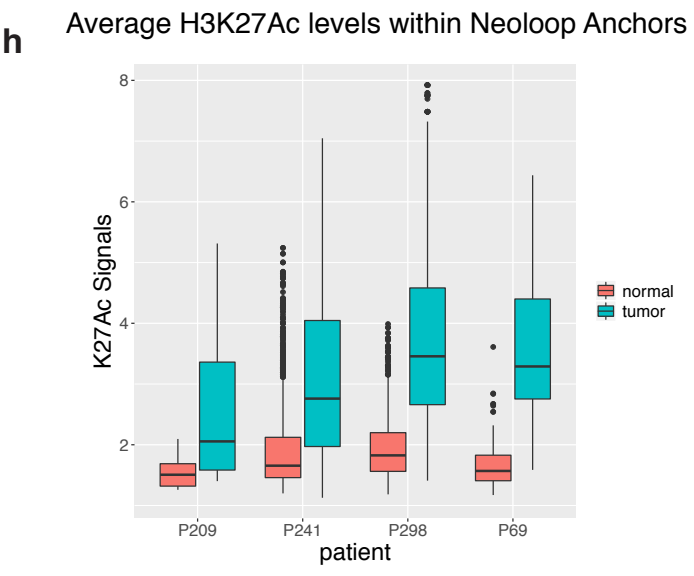




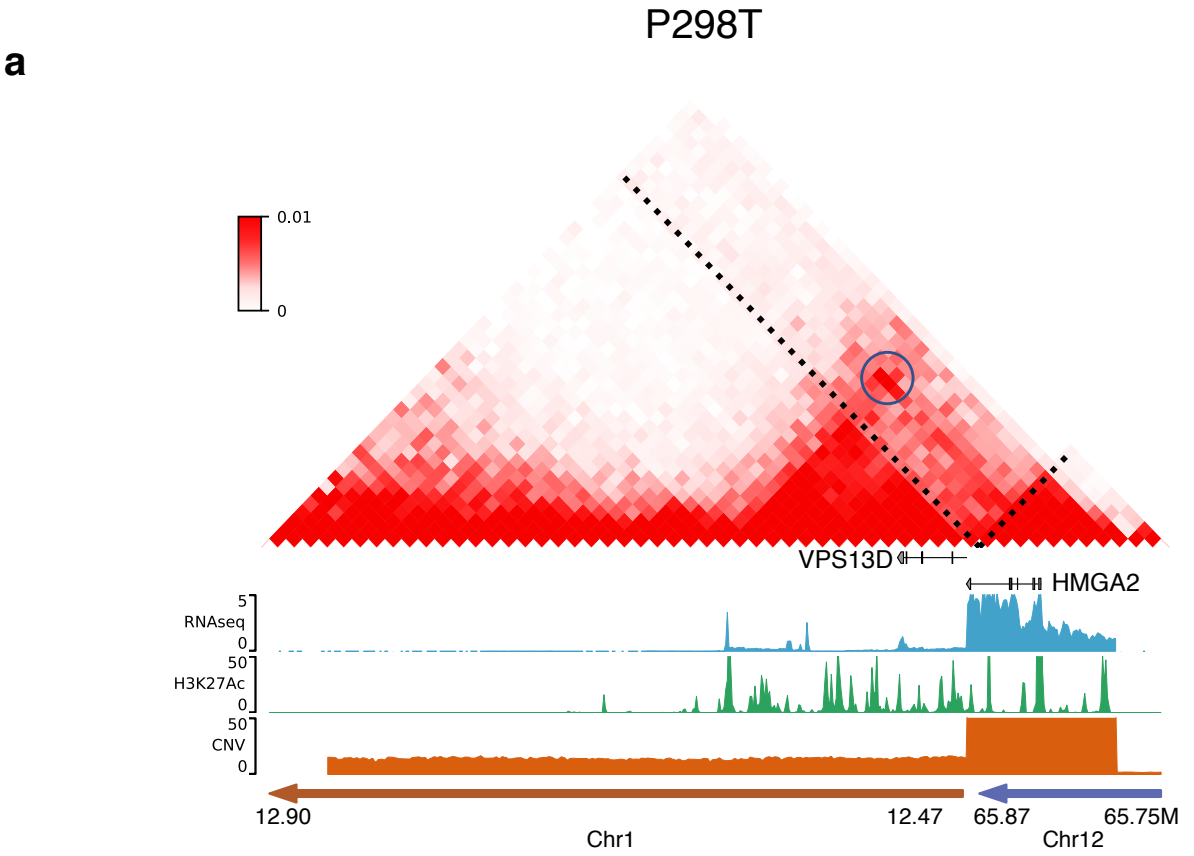


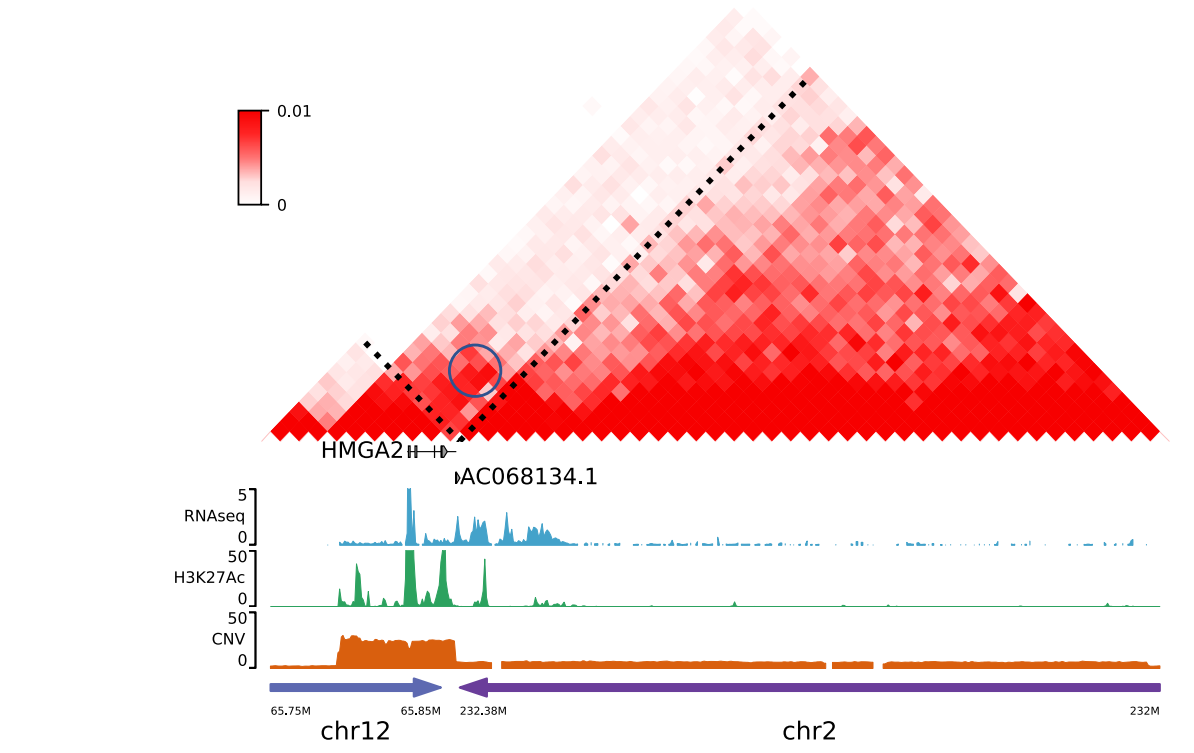




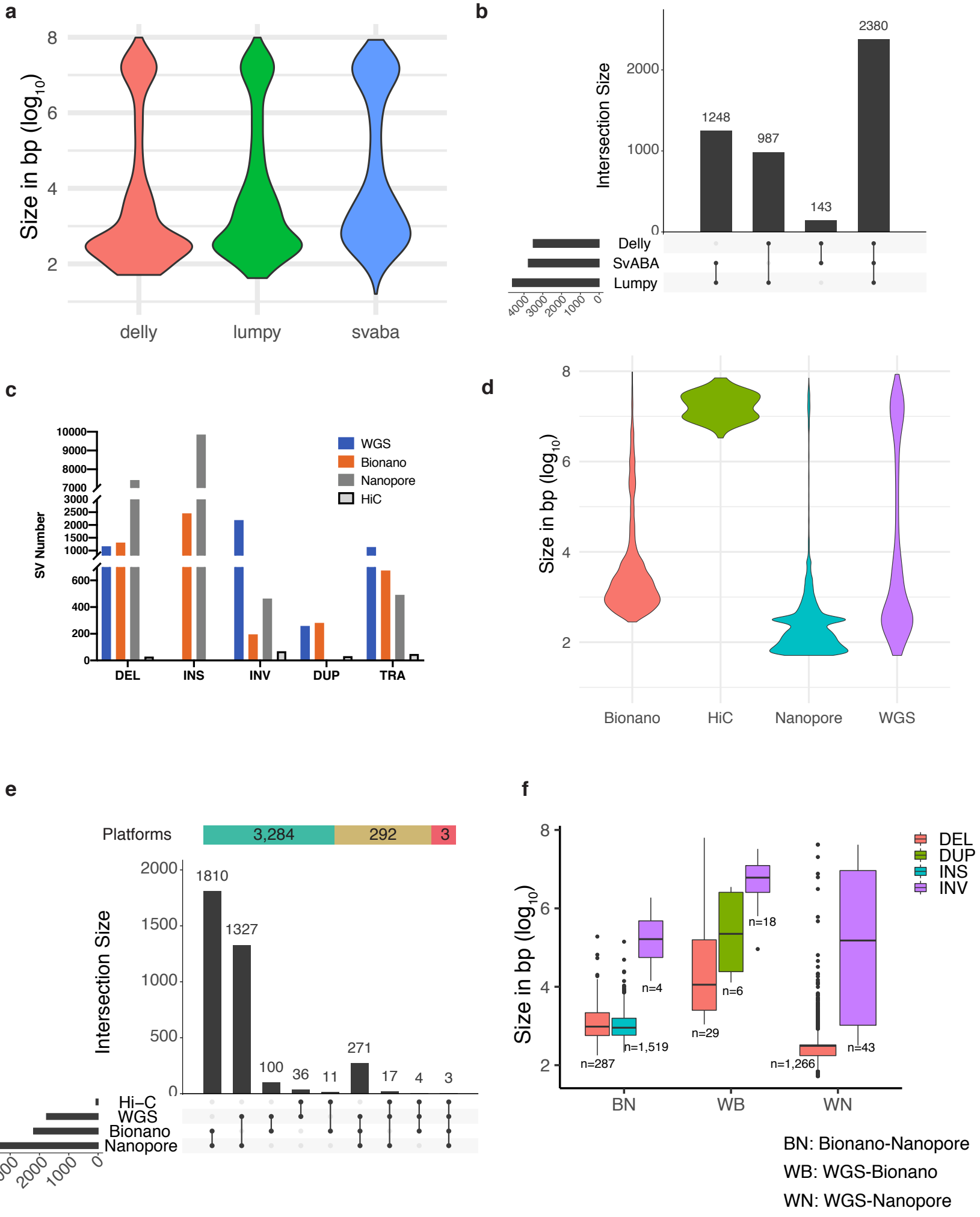


Supplementary Figure 7. Enhancer hijacking events in LPS. a, b. The reconstructed Hi-C map and ChIP-seq, RNA-seq and WGS tracks for two inversion events. **c, d**. The reconstructed Hi-C map with merged normal samples for the same regions as in A and B. **e, f**. The reconstructed Hi-C map for P241T and merged normal samples. **g**. Aggregated peak analysis for P241T and merged normal samples on 1440 neoloops identified from P241T. **h**. The boxplot for the Average H3K27Ac levels within neo-loop anchors.

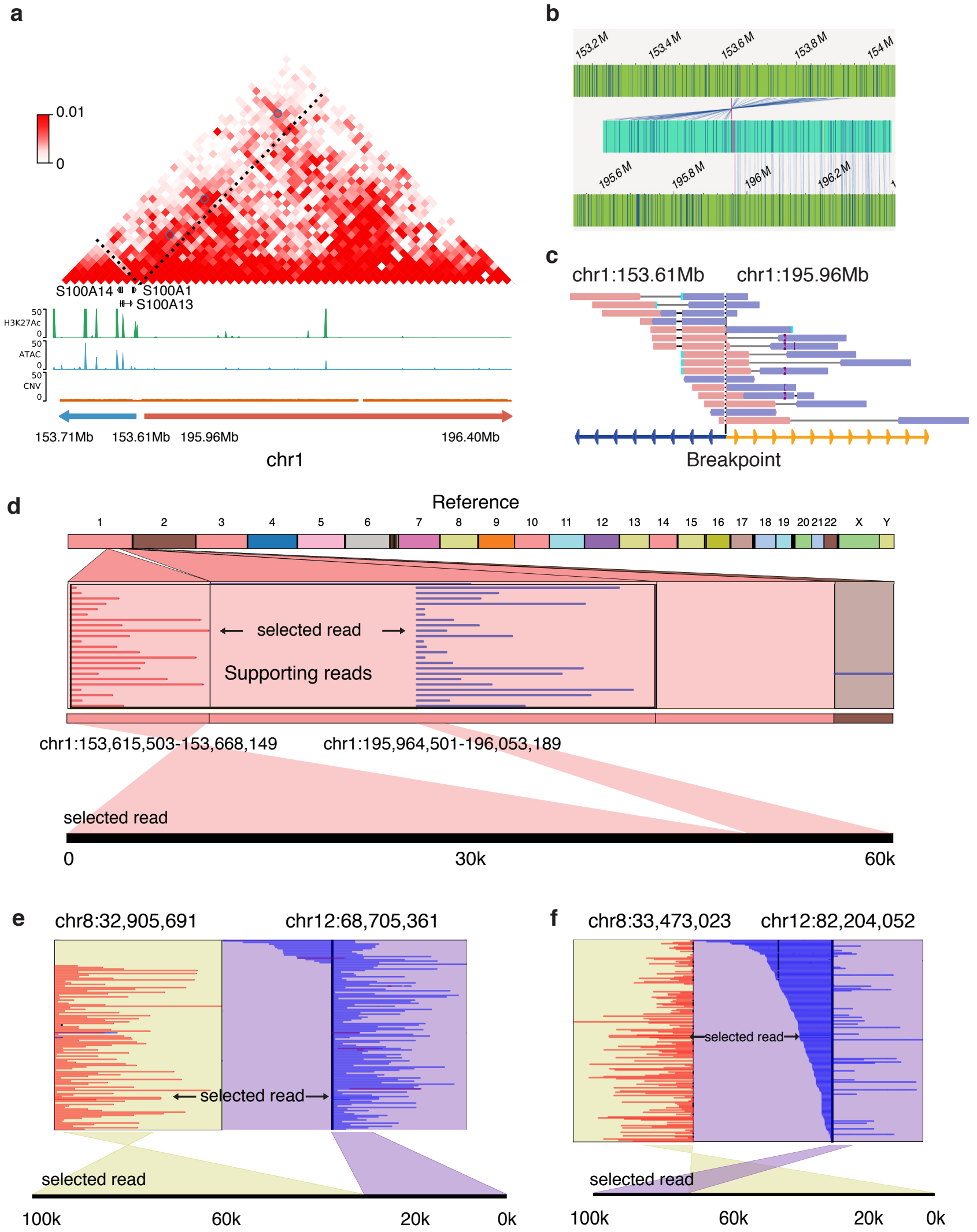




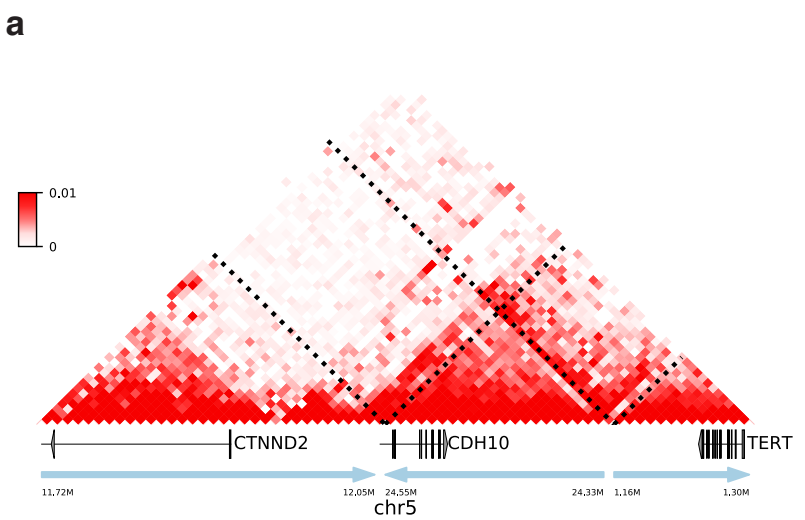
Supplementary Figure 8. Hi-C identified gene fusion events in LPS patients. a, b. The reconstructed Hi-C map and ChIP-seq, RNA-seq and WGS tracks for the HMGA2-VPS13D and HMGA2-AC068134.1 fusion events in P298 and P241, respectively.

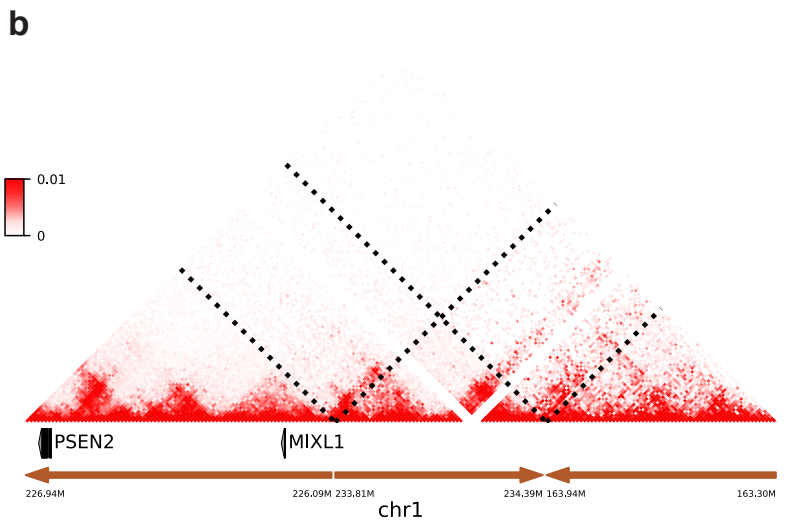


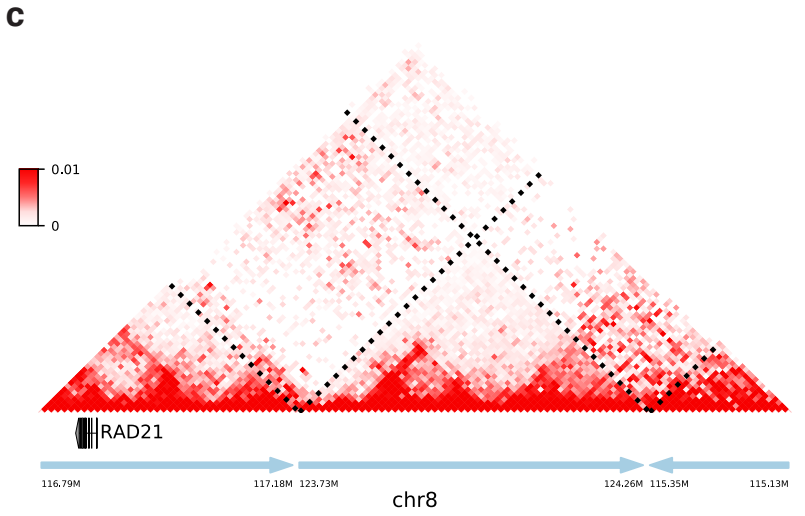
Supplementary Figure 9. The identification of the high-confidence list of SVs in Lipo863B. a. The SV size distribution from WGS dataset using different SV callers including Delly, Lumpy and SvABA. **b**. UpSet plot demonstrating the consensus SV list from different WGS SV callers. **c**. The stratified number of SVs identified from WGS, Bionano, Nanopore and Hi-C. **d**. The SV length distributions for each platform. Inter-chromosomal translocation events were excluded. **e.** UpSet plot demonstrating the high-confidence list of SVs, which supported by at least two platforms. **f**. The number of SVs and SV size distribution from the Bionano-Nanopore, WGS-Bionano and WGS-Nanopore overlapped set.

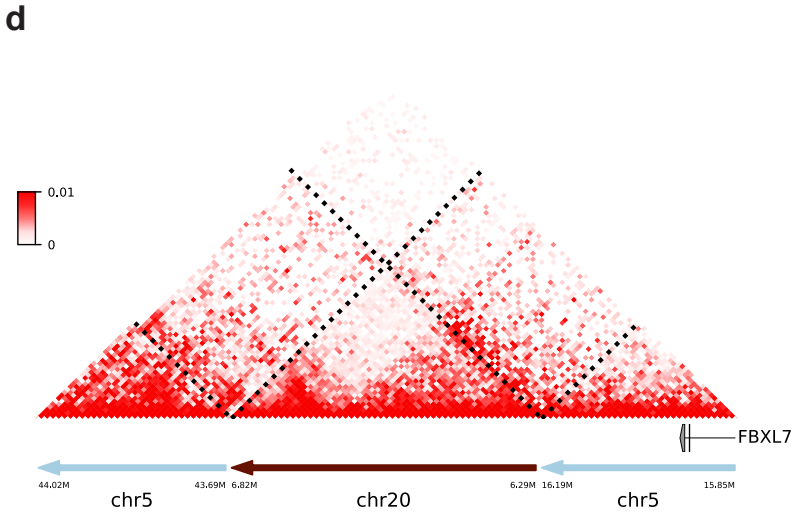


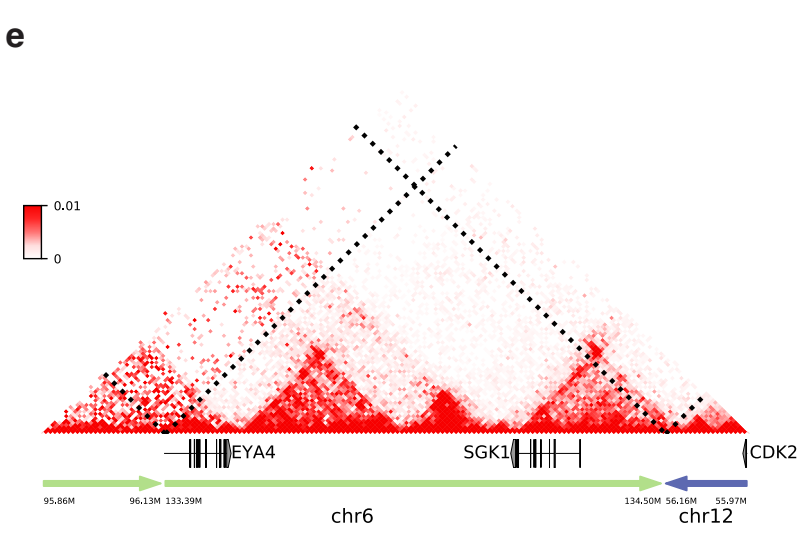
Supplementary Figure 10. The identification of the high-confidence list of SVs in Lipo863B. a-d. An example inversion event (chr1:153.61Mb, chr1:195.96Mb) from the high-confidence SVs supported by all 4 platforms: Hi-C (a), Bionano (b), WGS (c) and Nanopore (d). **e, f**. Supporting evidence from Nanopore for the junction points 2 and 3 in the main figure 5 c.

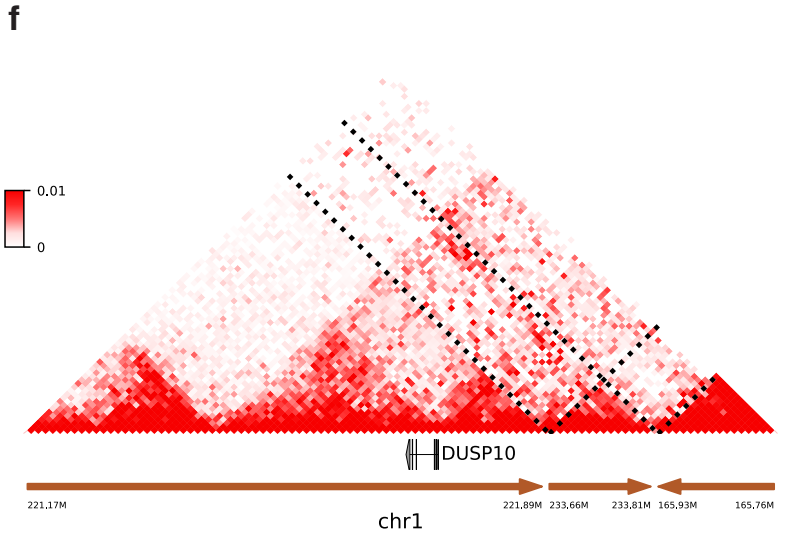




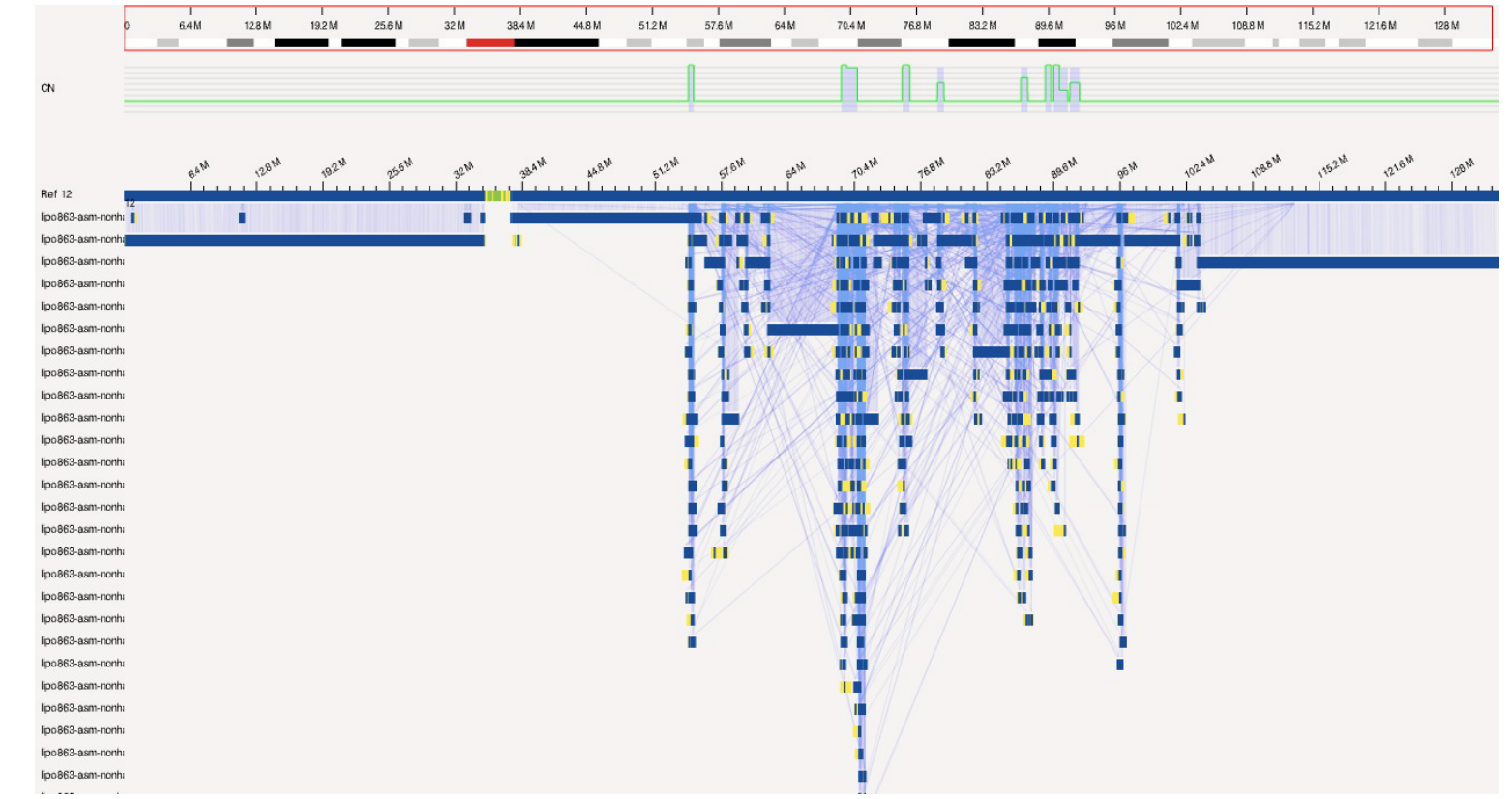


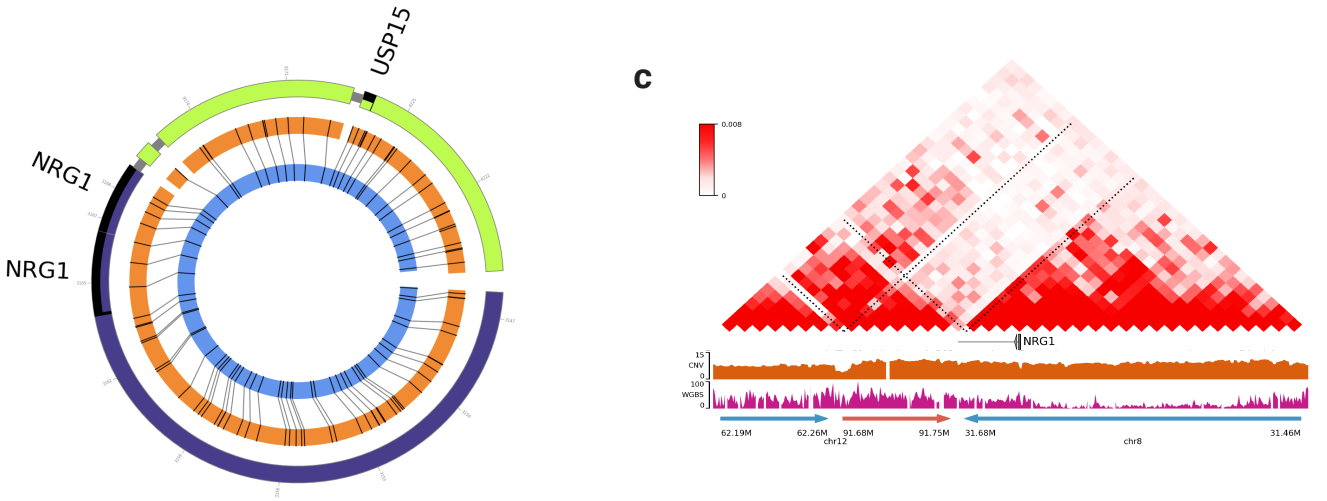


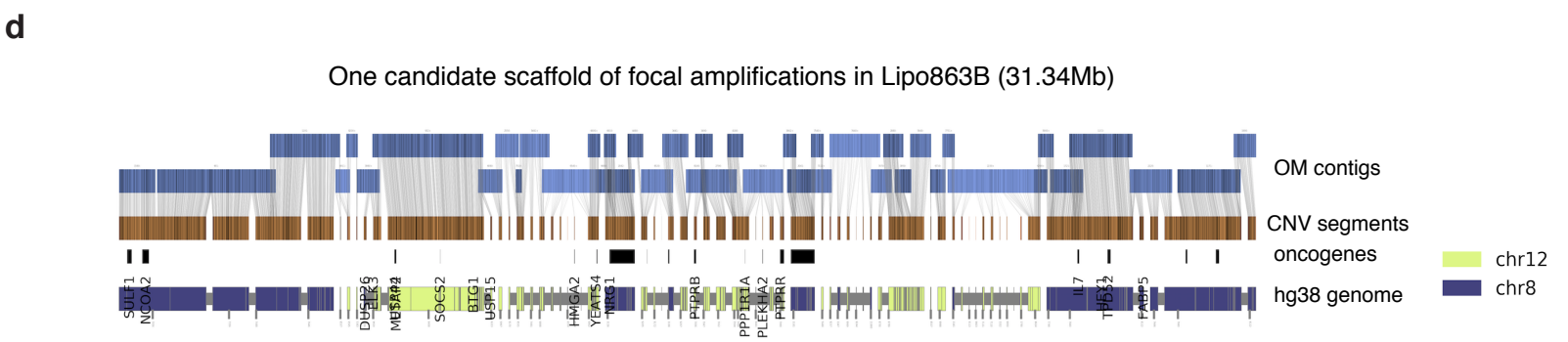




Supplementary Figure 11. Examples of complex SV reconstructions. a-f. The complex SV reconstructions from Hi-C data.





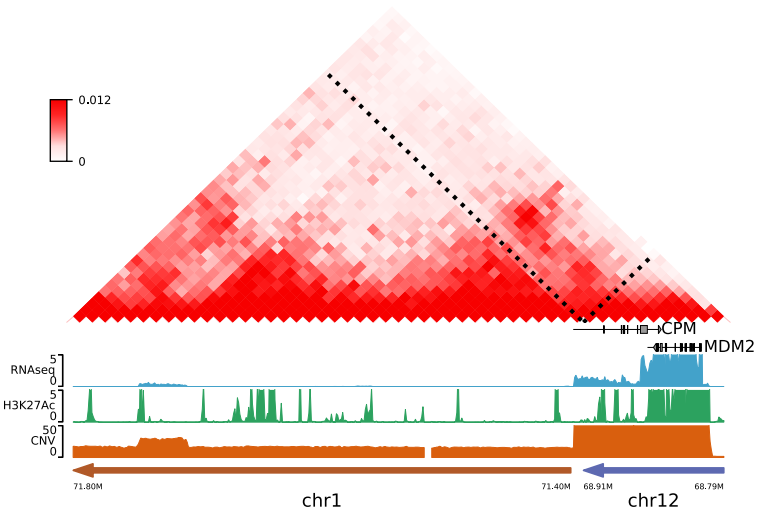


Supplementary Figure 12. Examples of complex SV reconstructions. a. Bionano assembled contigs aligned to the reference genome chr12. Heavily rearranged regions of the reference genome will show alignments from multiple contigs as demonstrated here from ~55-102Mb region. Contigs in yellow are not aligned to the displayed reference chromosome. **b**. Genome reconstruction based on Bionano and WGS. The outer circle is the corresponding genomic regions (chr8: dark blue, chr12: light green). The middle circle in yellow are the CNV segments from WGS data. The inner blue circle is the Bionano contig. **c**. The Hi-C map corresponding to the reconstruction in (b). **d**. The candidate scaffold of focal amplifications in Lipo863B using WGS and Bionano data. The top blue panel shows the Bionano contigs, middle panel are the CNV segments identified from WGS data.

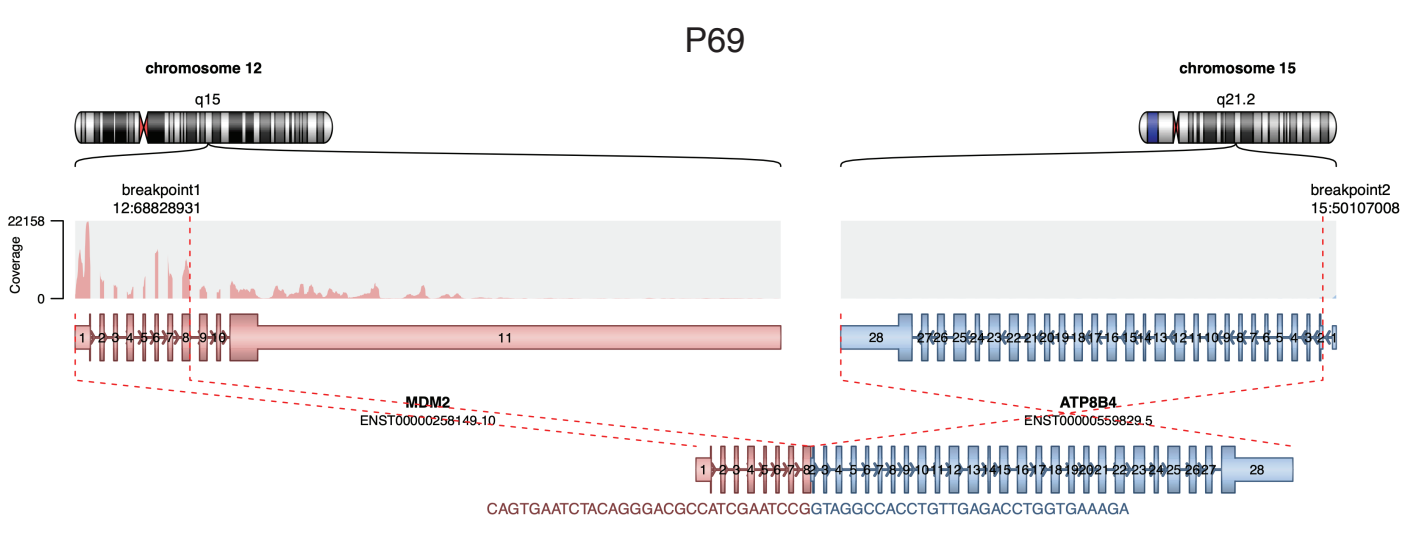
a

	Up	fusion	Co-amp	hijack
P298	Yes	Yes	Yes	Yes
P241	Yes	No	Yes	No
P69	Yes	Yes	Yes	Yes
P209	Yes	Yes	Yes	No

b



c



Supplementary Figure 13. Co-occurrence of events for MDM2 in patients. a. Occurrence of up-regulation, gene fusion, co-amplification and enhancer hijacking events for MDM2 in patient samples . **b**. Example of enhancer hijacking events in P298 for MDM2. **c**. Gene fusion events for MDM2 in P69.