

SUPPLEMENTAL APPENDIX

Supplement to: Multi-omic analysis and immunoprofiling reveals distinct subtypes of human angiosarcoma

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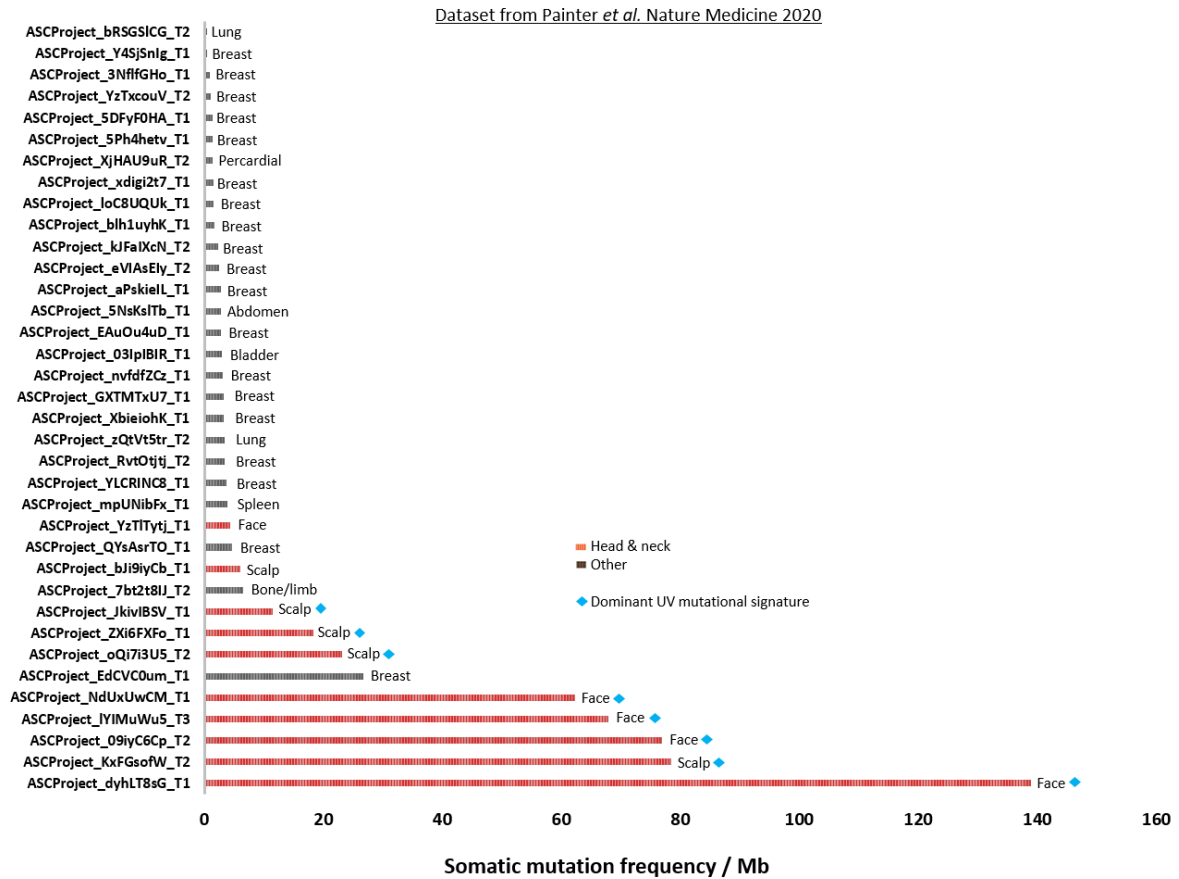
Supplemental Table S15. Quality control of whole genome sequencing data

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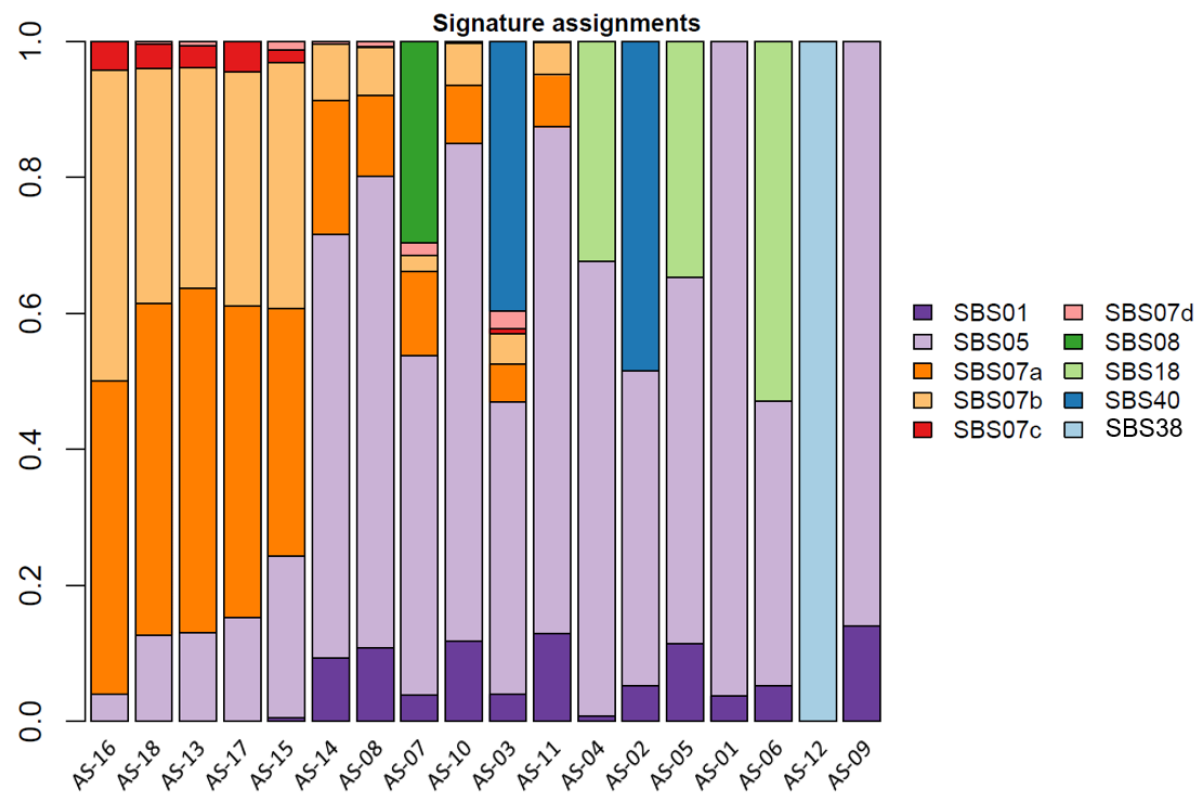
Supplemental Table S17. Primer sequences for polymerase chain reactions

1.0 Supplemental Figures

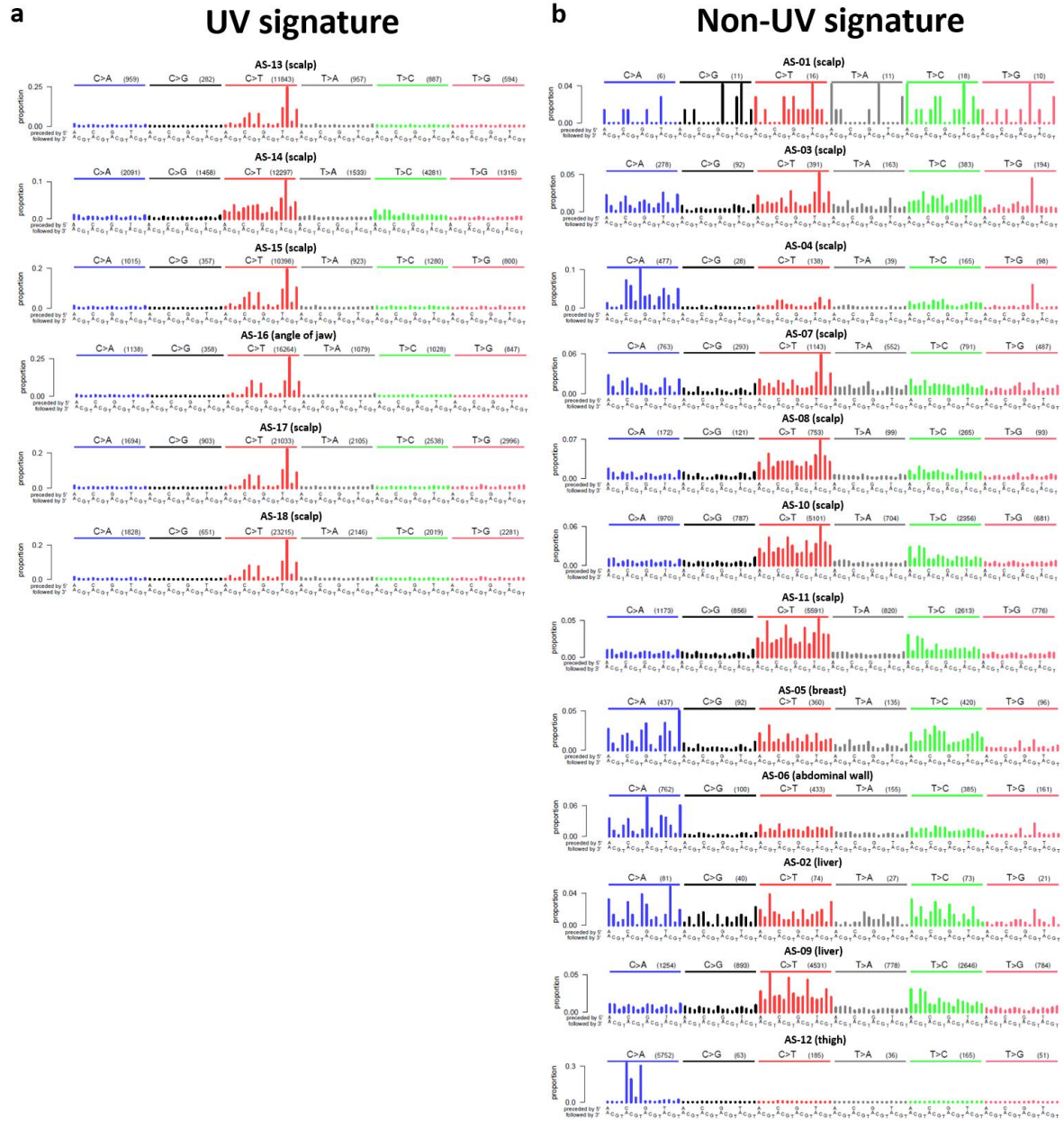
Supplemental Figure S1. Somatic mutation frequency of angiosarcoma samples in the cohort of Painter *et al.*, Nature Medicine 2020.



Supplemental Figure S2. Signature assignments of angiosarcomas.

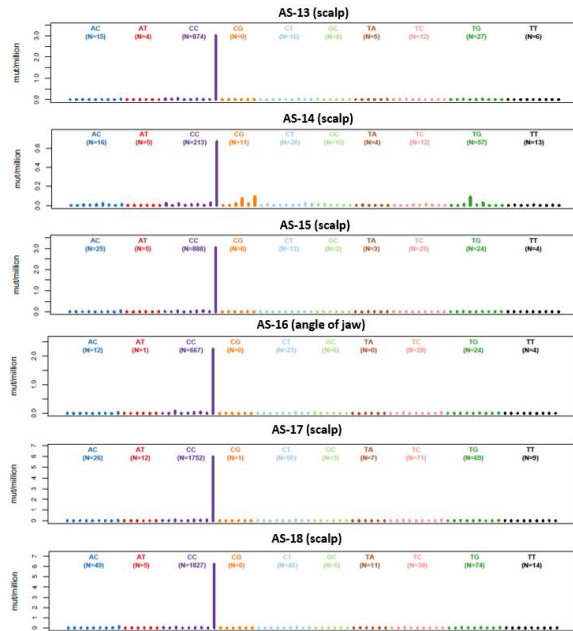


Supplemental Figure S3. Mutational signatures of angiosarcomas. Overall trinucleotide context of all mutations are shown for cases with (A) UV signatures and (B) non-UV signatures

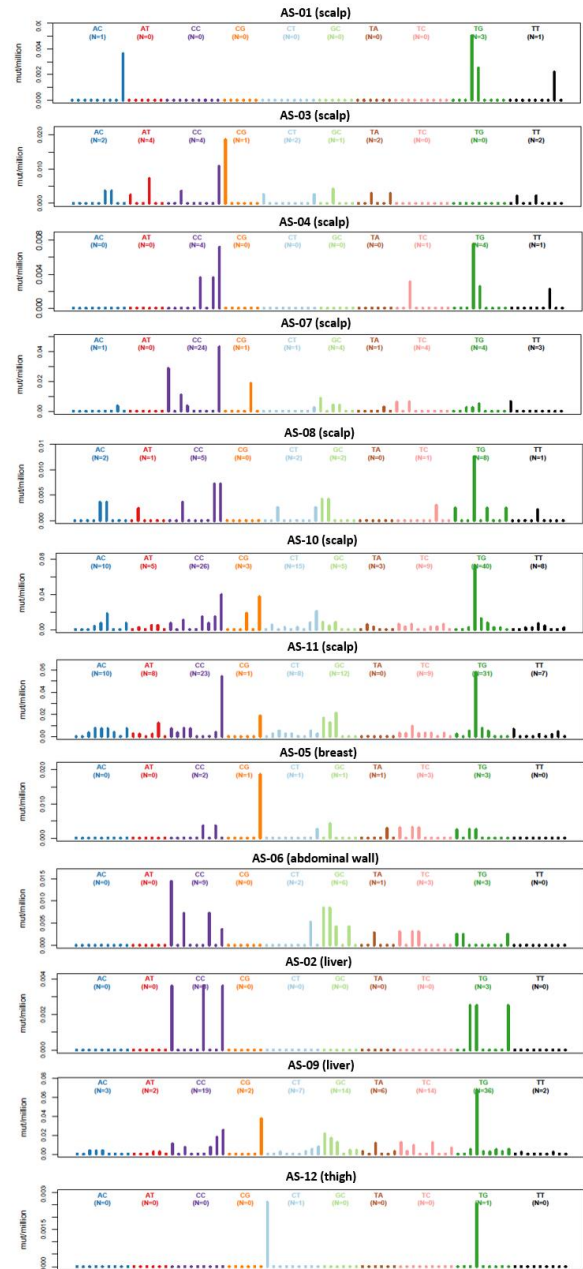


Supplemental Figure S4. Dinucleotide base substitutions in angiosarcomas. (A) UV signatures and (B) Non-UV signatures.

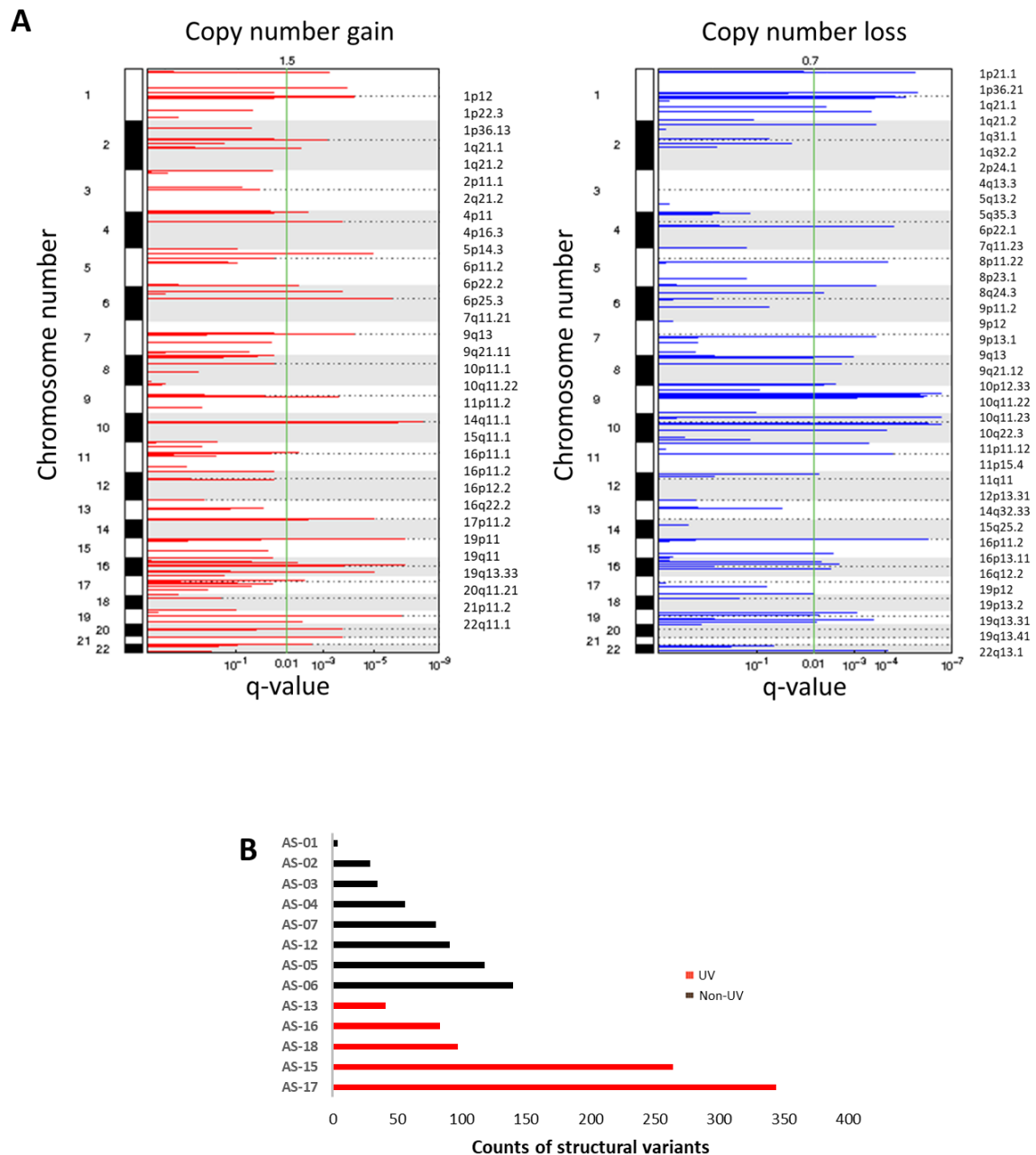
a UV signature



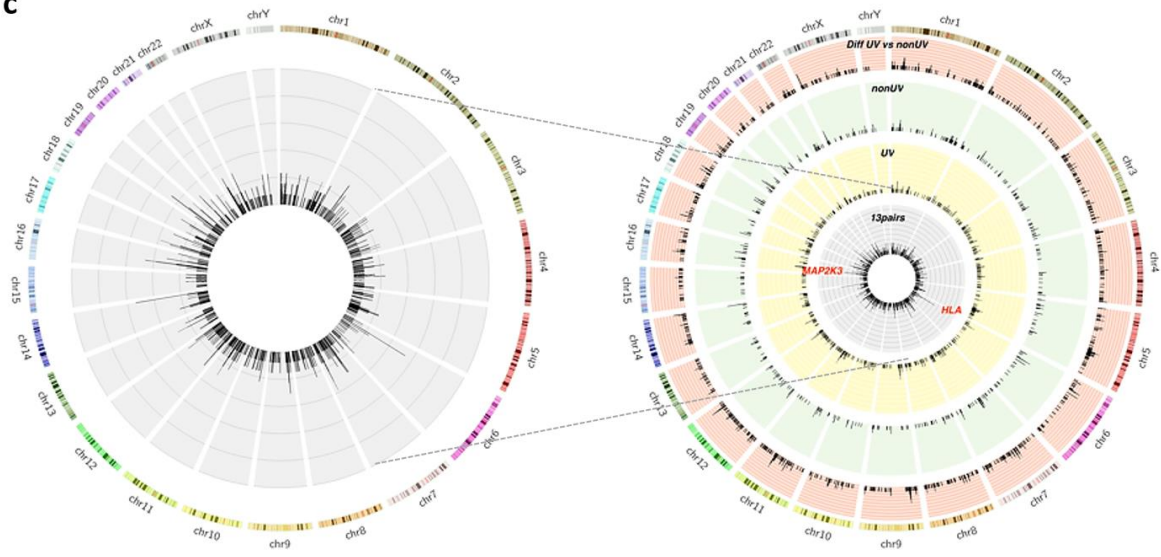
b Non-UV signature



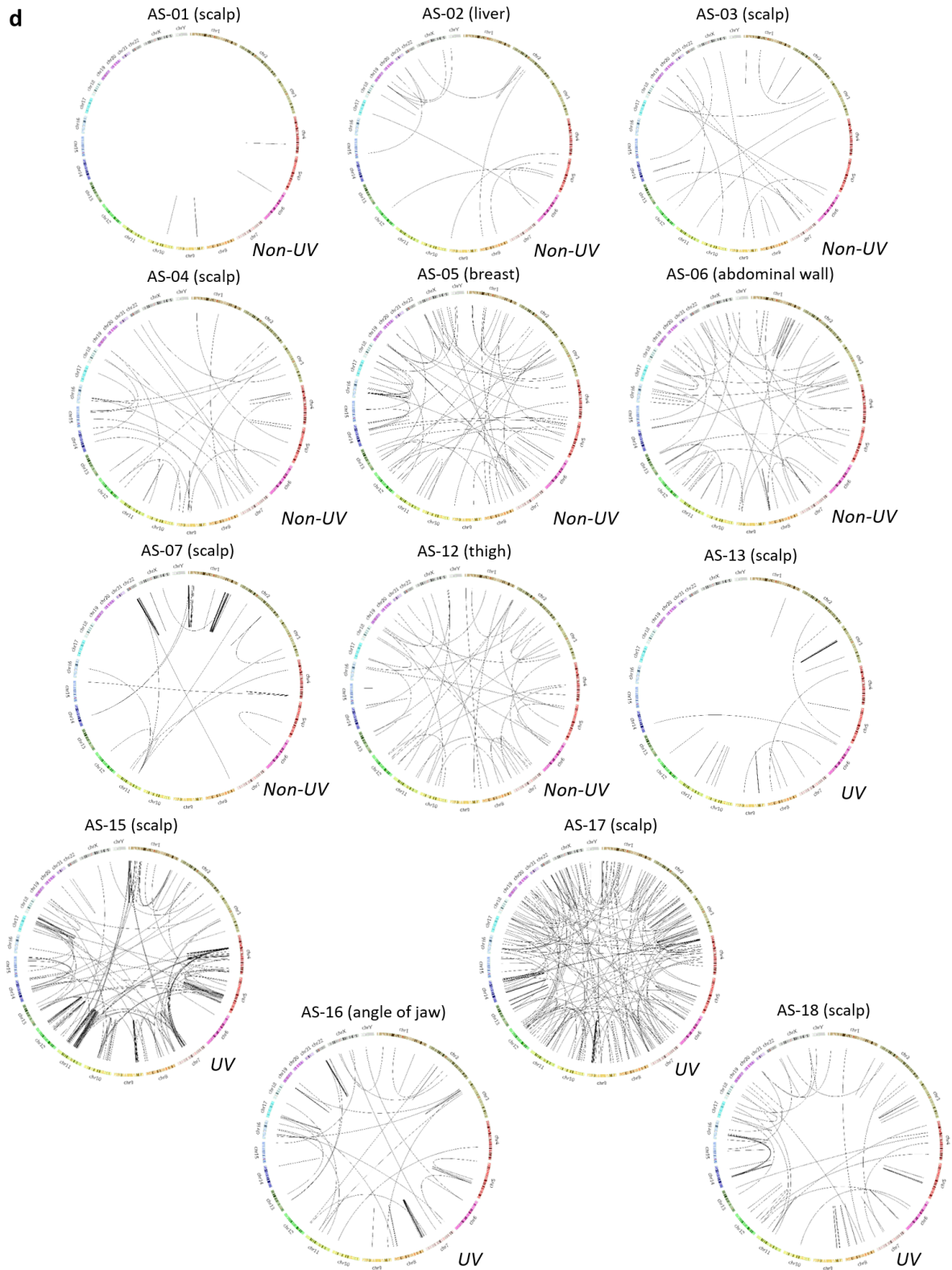
Supplemental Figure S5. Copy number alterations and structural variants in angiosarcomas. (A) Analysis of somatic copy-number alterations identified 37 gained genomic and 68 lost regions. (B) Structural variant counts. (C) Recurrent structural rearrangements observed include those in the chromosome 6 region harboring the human leukocyte antigen (*HLA*) complex and chromosome 17 region harboring *MAP2K3*. (D) Structural variations of individual cases represented as Circos plots.

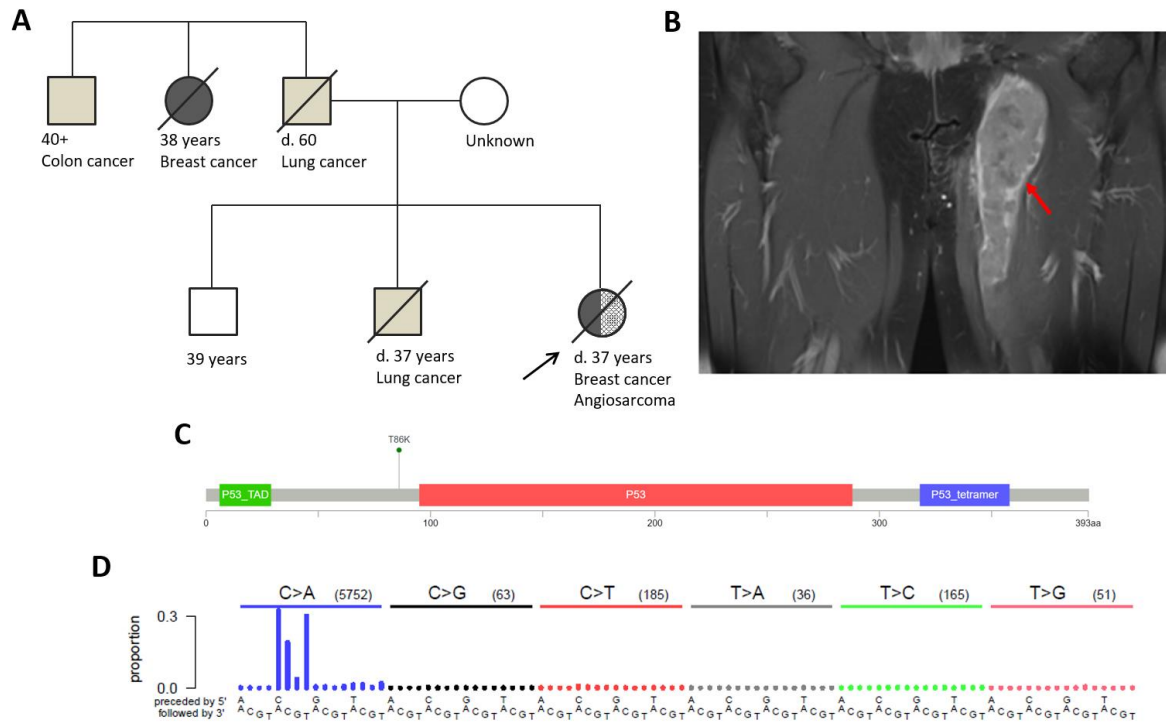


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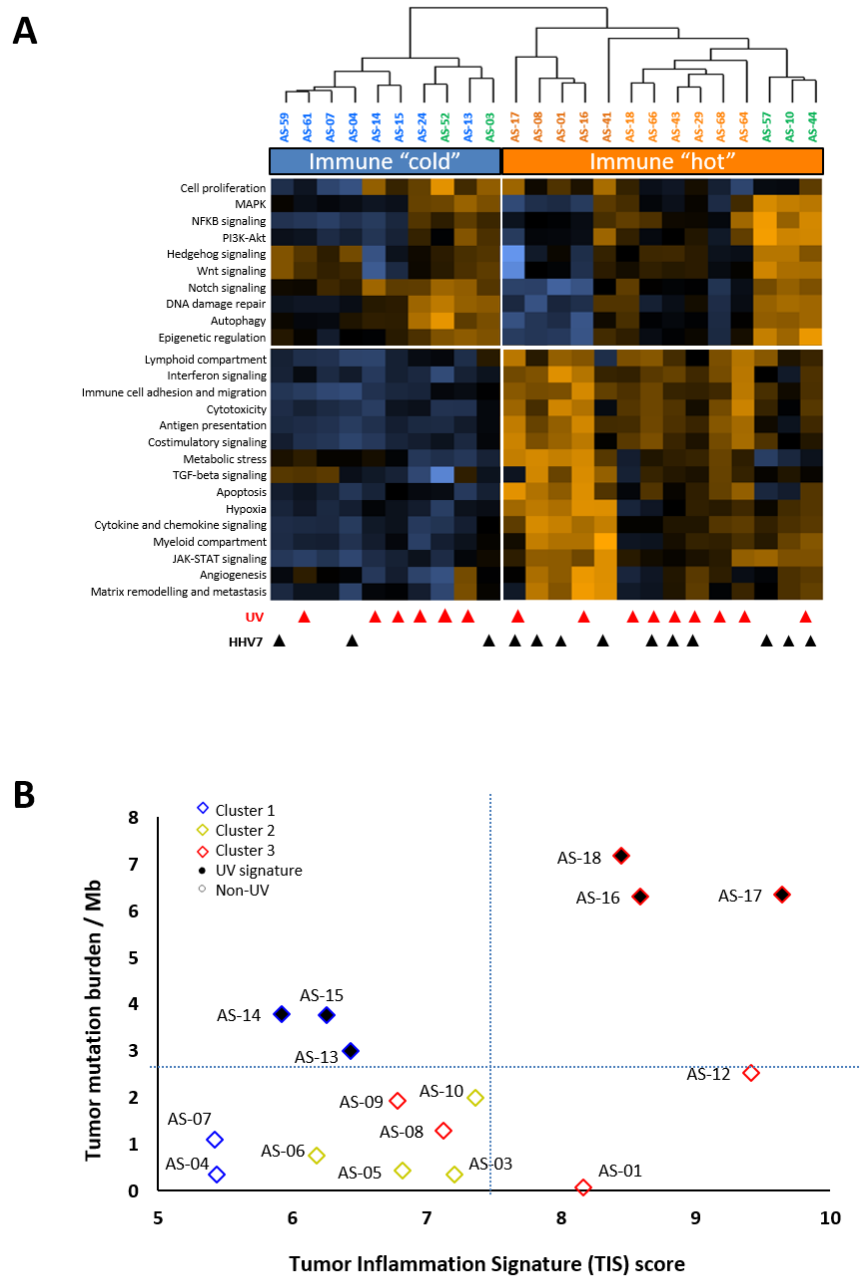


d

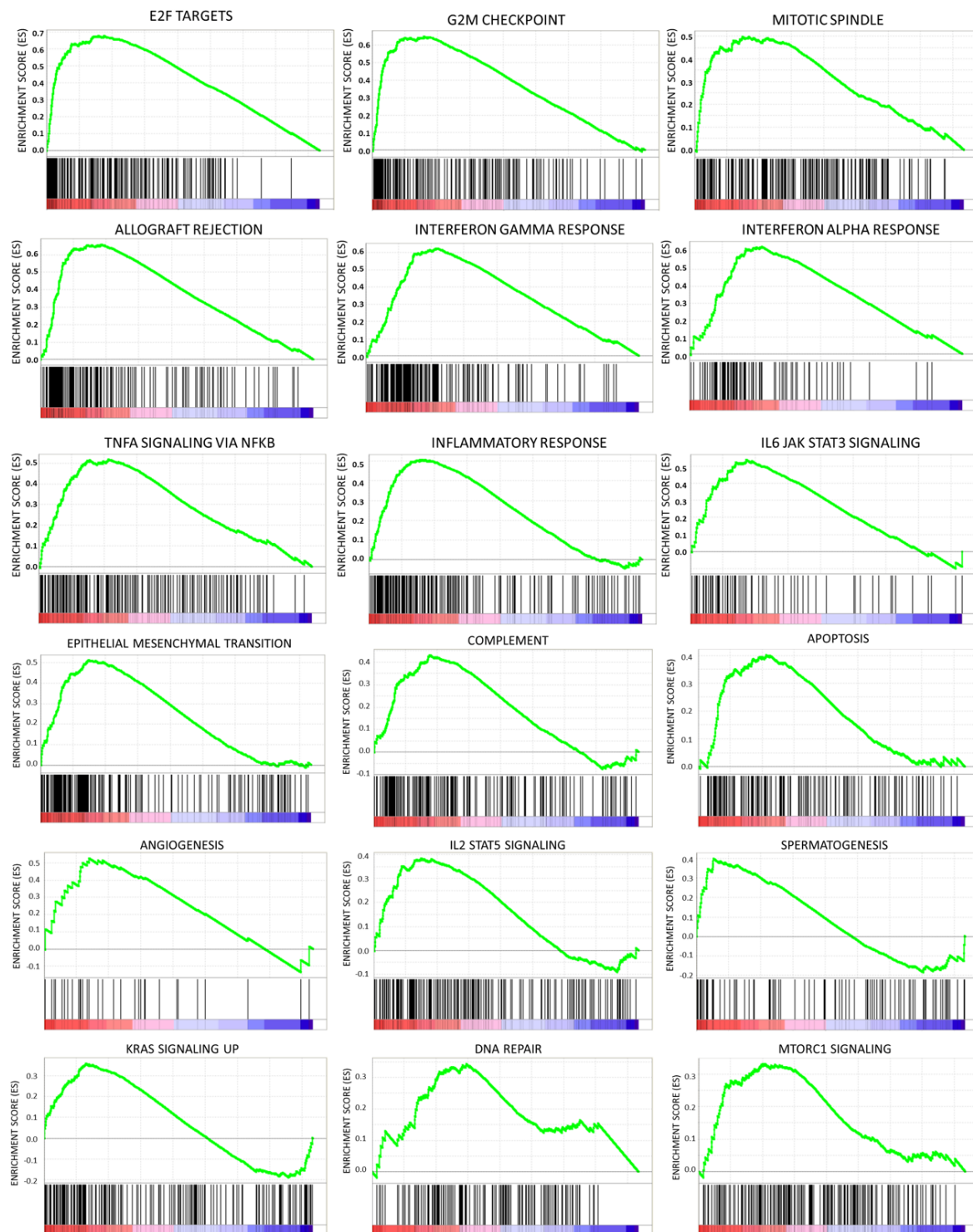


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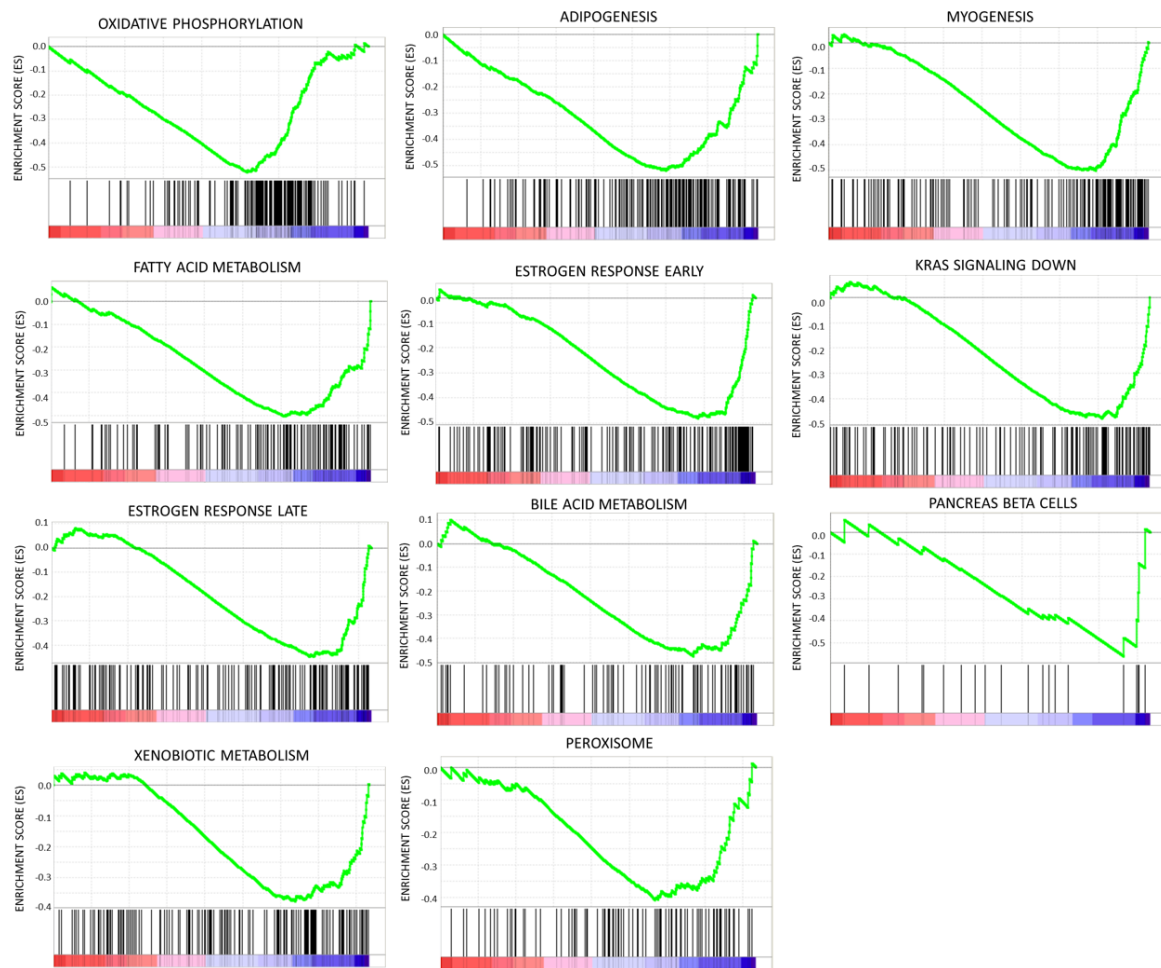
Supplemental Figure S7. Additional data from NanoString profiling. (A) Including only angiosarcoma of the head and neck, 2 distinct clusters could be identified based on immune-related signals, into immune “cold” or “hot” subgroups. This classification was largely in keeping with the clustering results incorporating all samples. Cluster 1 cases (blue) and Cluster 3 cases (orange) were expectedly grouped as immune “cold” and “hot”, respectively. Cluster 2 cases (green) were redistributed into immune “cold” or “hot” groups. (B) Angiosarcoma landscape defined by TMB and TIS scores.



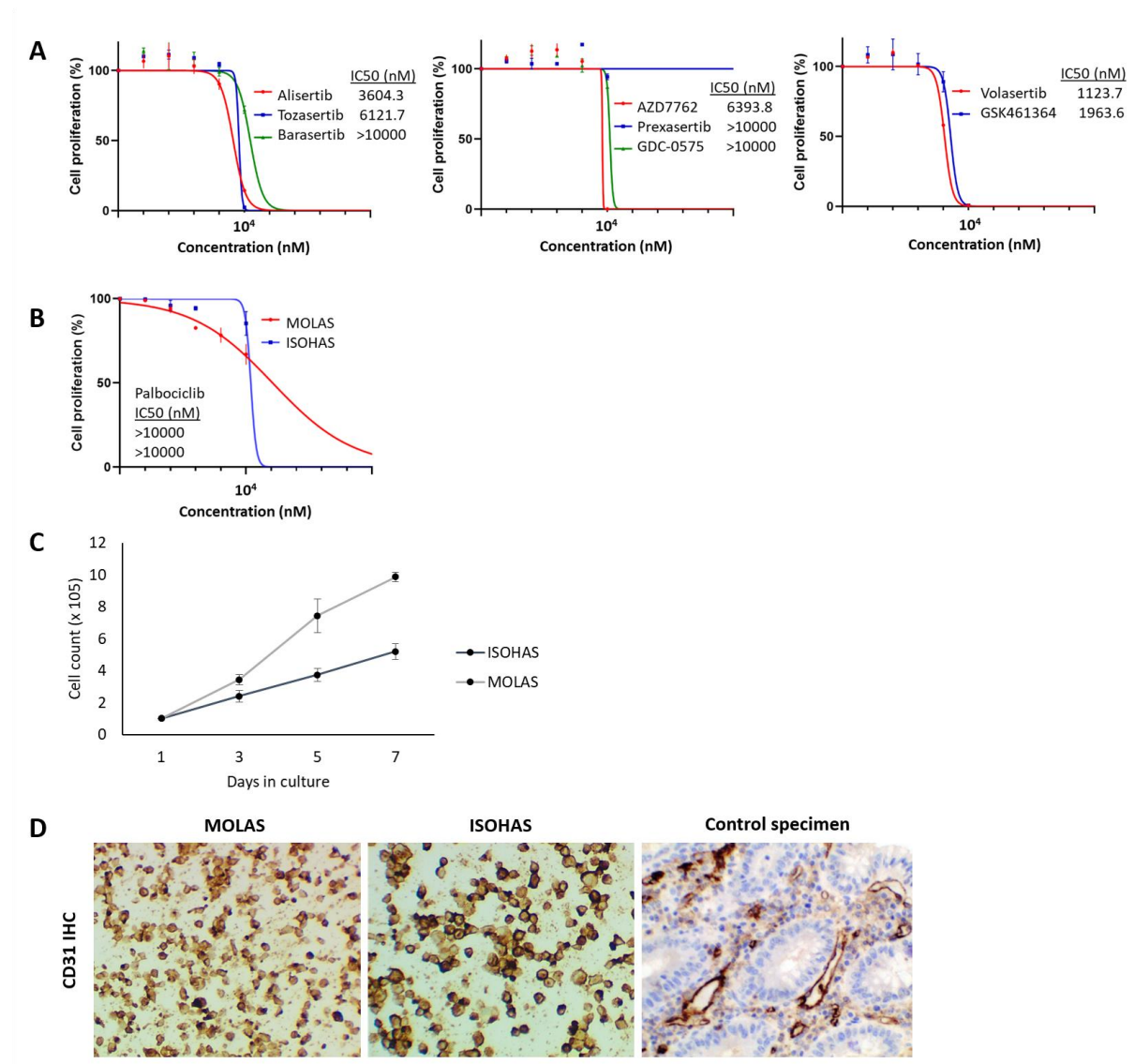
Supplemental Figure S8. Upregulated pathways in angiosarcoma tumor compared to normal tissue.



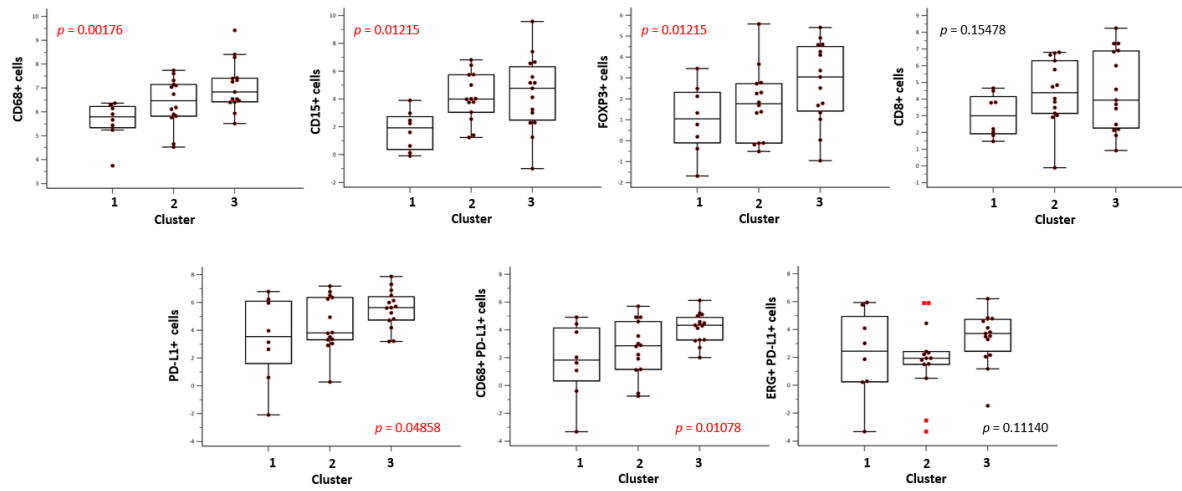
Supplemental Figure S9. Downregulated pathways in angiosarcoma tumor compared to normal tissue.



Supplemental Figure S10. Additional information on cell line experiments. (A) Relative lack of efficacy of kinase inhibitors in HDMEC cell line. (B) Palbociclib is ineffective in angiosarcoma cell lines MOLAS and ISOHAS. (C) Base line growth characteristic in culture without drug treatment. (D) CD31 immunostaining of both angiosarcoma cell lines. A control specimen demonstrating positive CD31 staining in the blood vessels but not the colonic epithelial cells is shown.

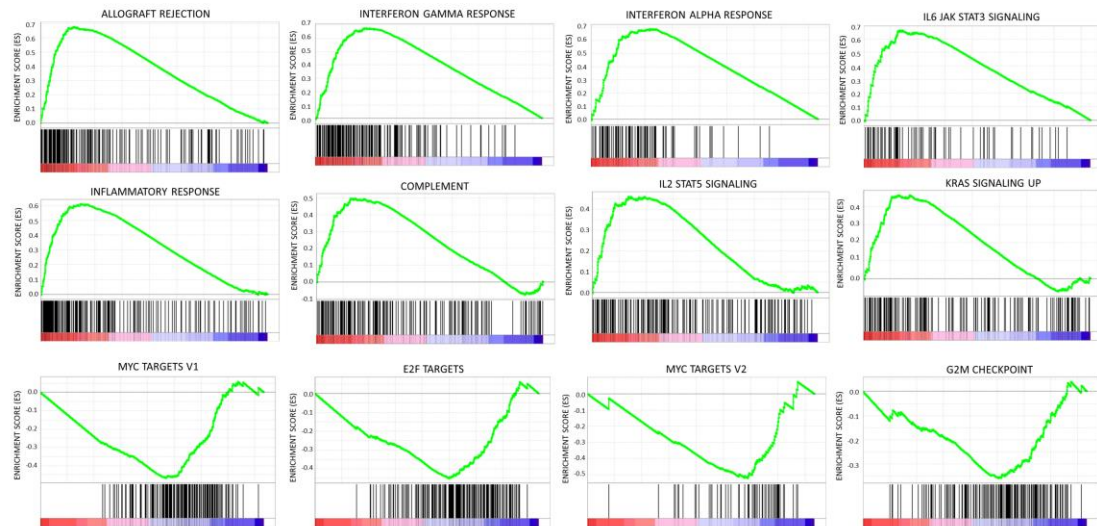


Supplemental Figure S11. Correlation of immune cell infiltrates with NanoString clusters.



Supplemental Figure S12. Altered pathways in HHV7-positive angiosarcoma compared to HHV7-negative cases. (A) Gene set enrichment analysis of RNA-seq data (disclosure: also included in part within Figure 6C) and (B) Pathway analysis of NanoString data.

A



B

