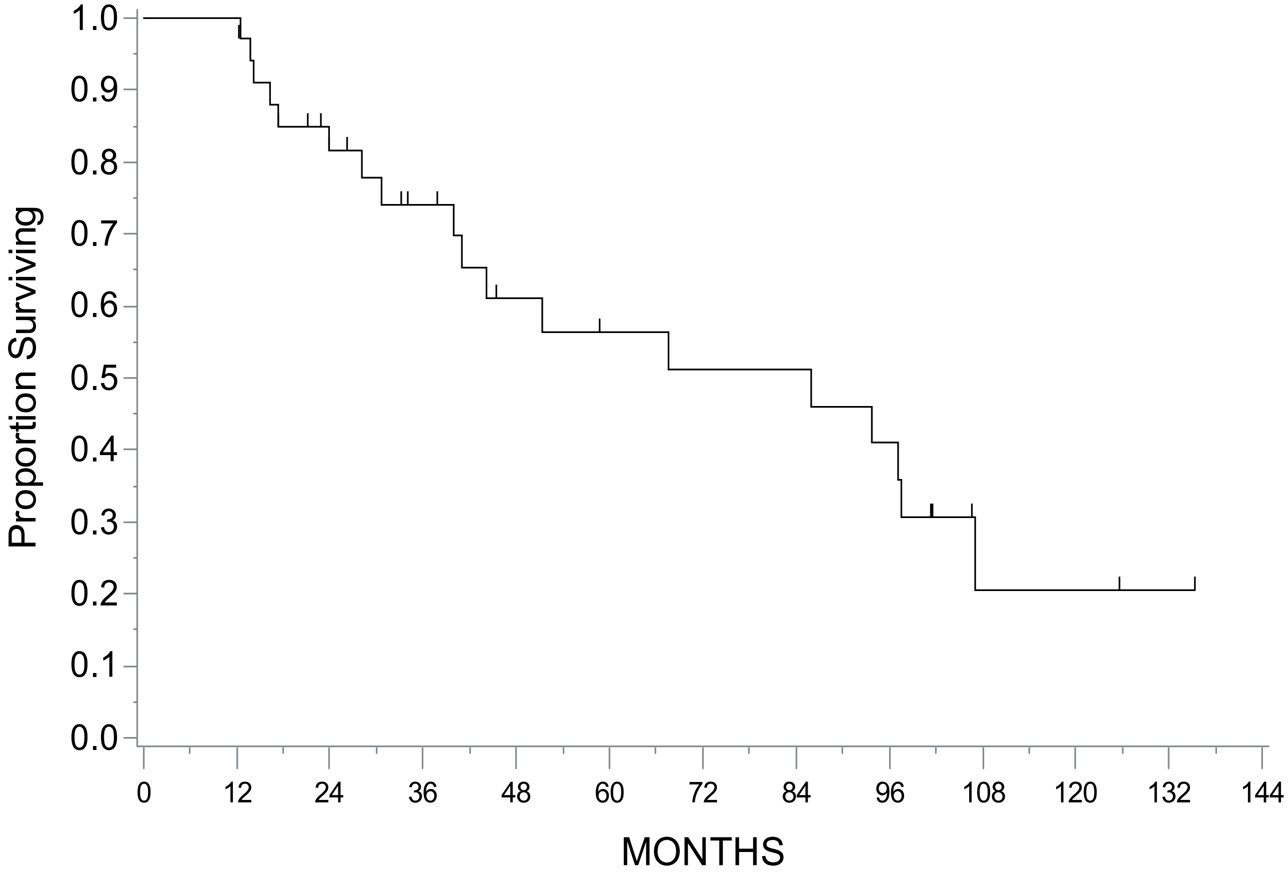
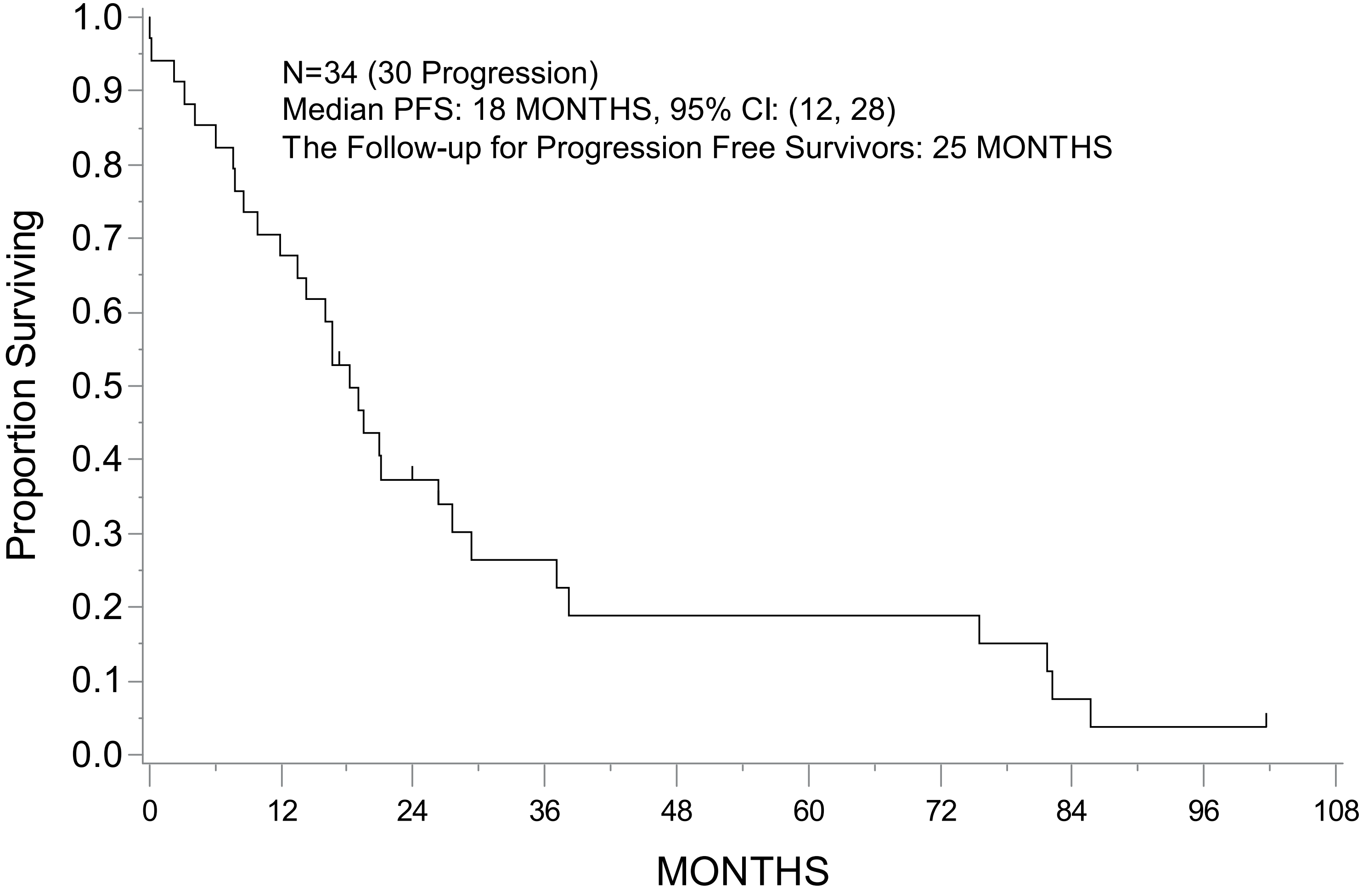
Supplemental Figures

Supplemental Figure S1A. Overall survival of acral cohort



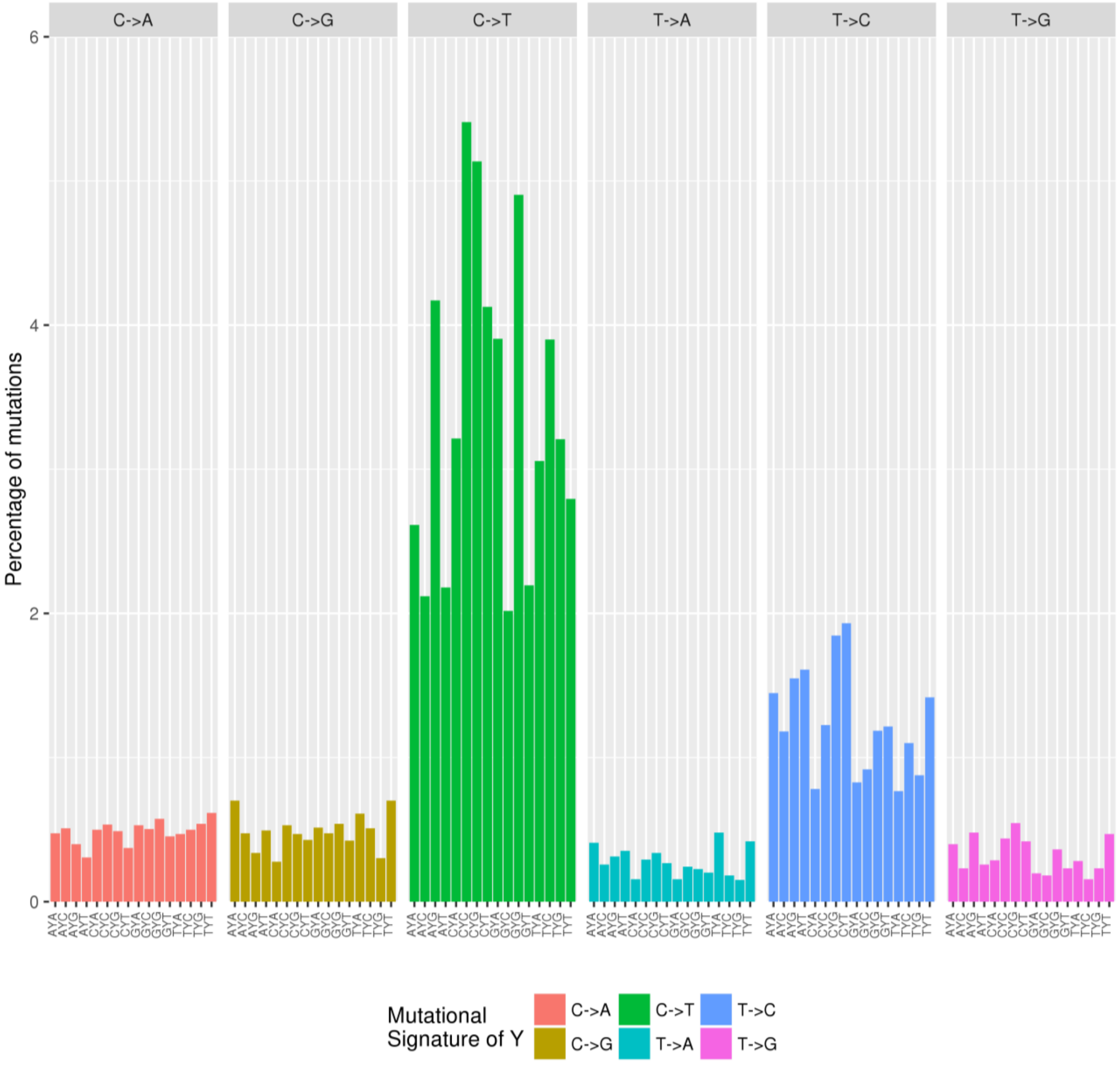
Median overall survival = 86 months
Median FUP survivors = 36 months

Supplemental Figure S1B. Overall progression-free survival of acral cohort



Supplemental Figure S2. SNV mutational signature of all tumors

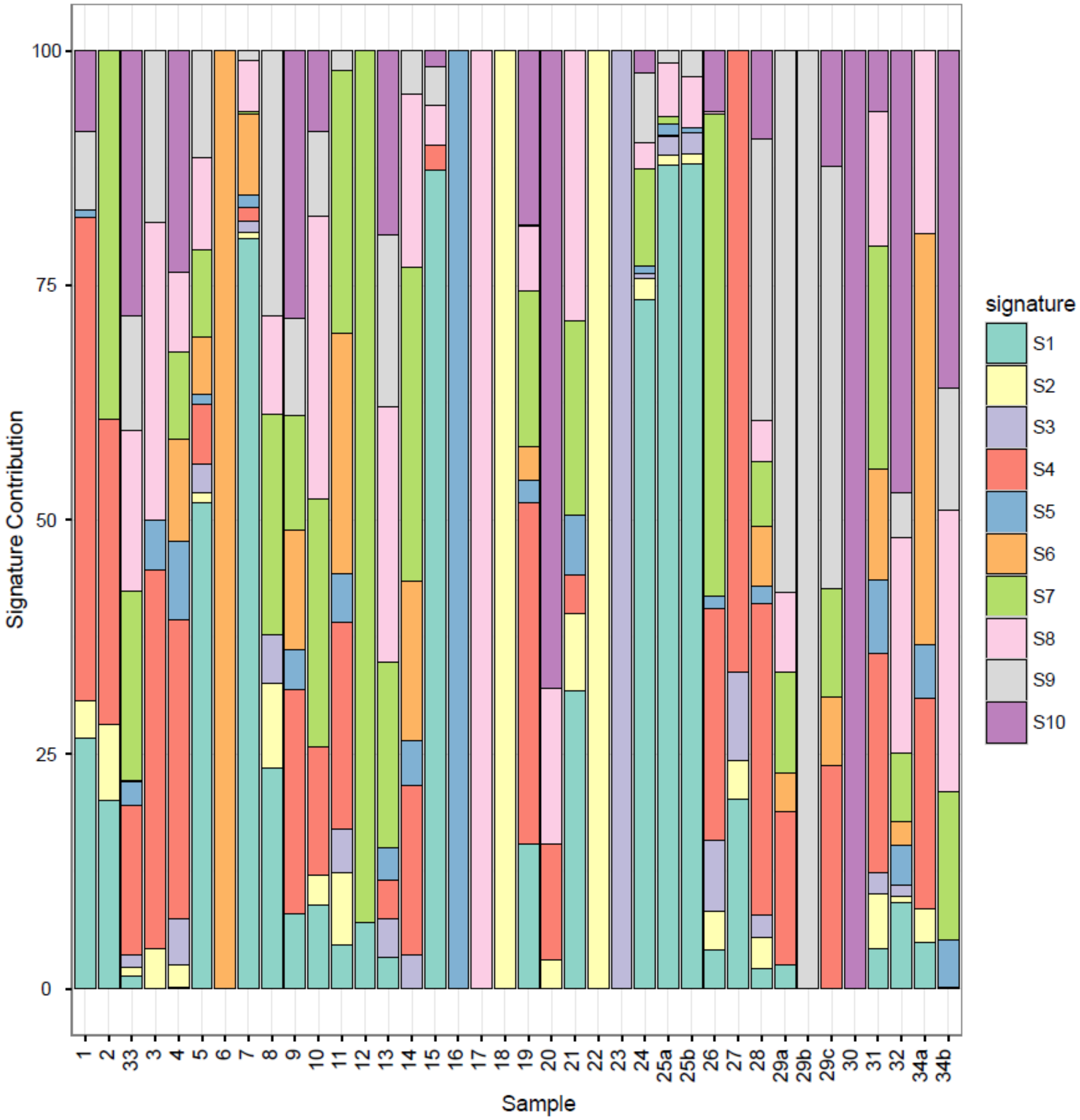
All substitutions are referred to by the pyrimidine context of the mutated Watson and Crick base pair. For all possible pyrimidine substitutions (Y), the flanking upstream and downstream bases are shown on the X-axis, thereby leading to 96 possible mutation contexts in the classification. The mutation base change is shown in the legend according to color.



Supplemental Figure S3. Somatic signature analysis

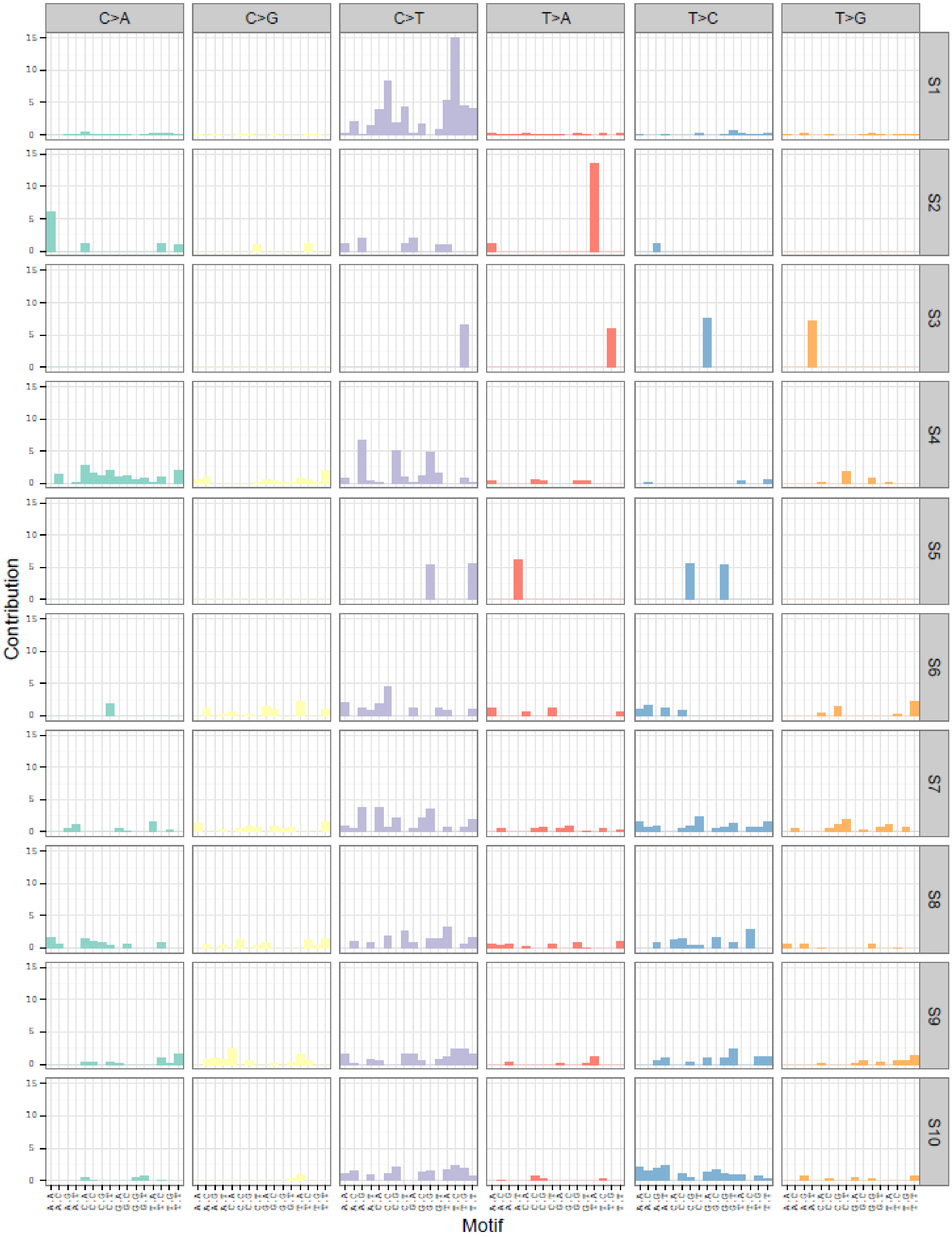
A. Breakdown of signatures across tumors

The distribution of ten somatic signatures, derived from SNVs, is shown across all samples.



B. SNV composition of identified signatures

Signature identifiers are shown on the right and the percent contribution of SNVs are shown on the left. The sequence context of each SNV is shown on the bottom.



Supplemental Figure S3. Tumor-specific SV/CNV summary plots

Individual Circos plots for each tumor are shown here with tumor-specific SVs and CNVs identified from LIWG analysis, and CNVs identified from exome analysis. The same gene labels are shown for each Circos plot to allow for cross-plot comparisons. Gene labels include those shown in Figure 2B, in addition to partner genes for identified TERT SVs.

CNVs are shown in the inner circle adjacent to chromosomes: exome CNV gain=red, LIWG CNV gain=green, exome CNV loss=blue, LIWG CNV loss=orange. The scale for CNV changes are static across all Circos plots with a threshold of log2 fold=|4| to allow for cross-plot comparisons. No filtering was applied to CNV data shown here.

Intrachromosomal SVs=gray (for SVs < 1Mb), green (for SVs >=1Mb & <50Mb), black (for SVs >=50Mb & <100Mb), red (for SVs >=100Mb); Interchromosomal SVs=red; Interchromosomal SVs impacting chr5=yellow

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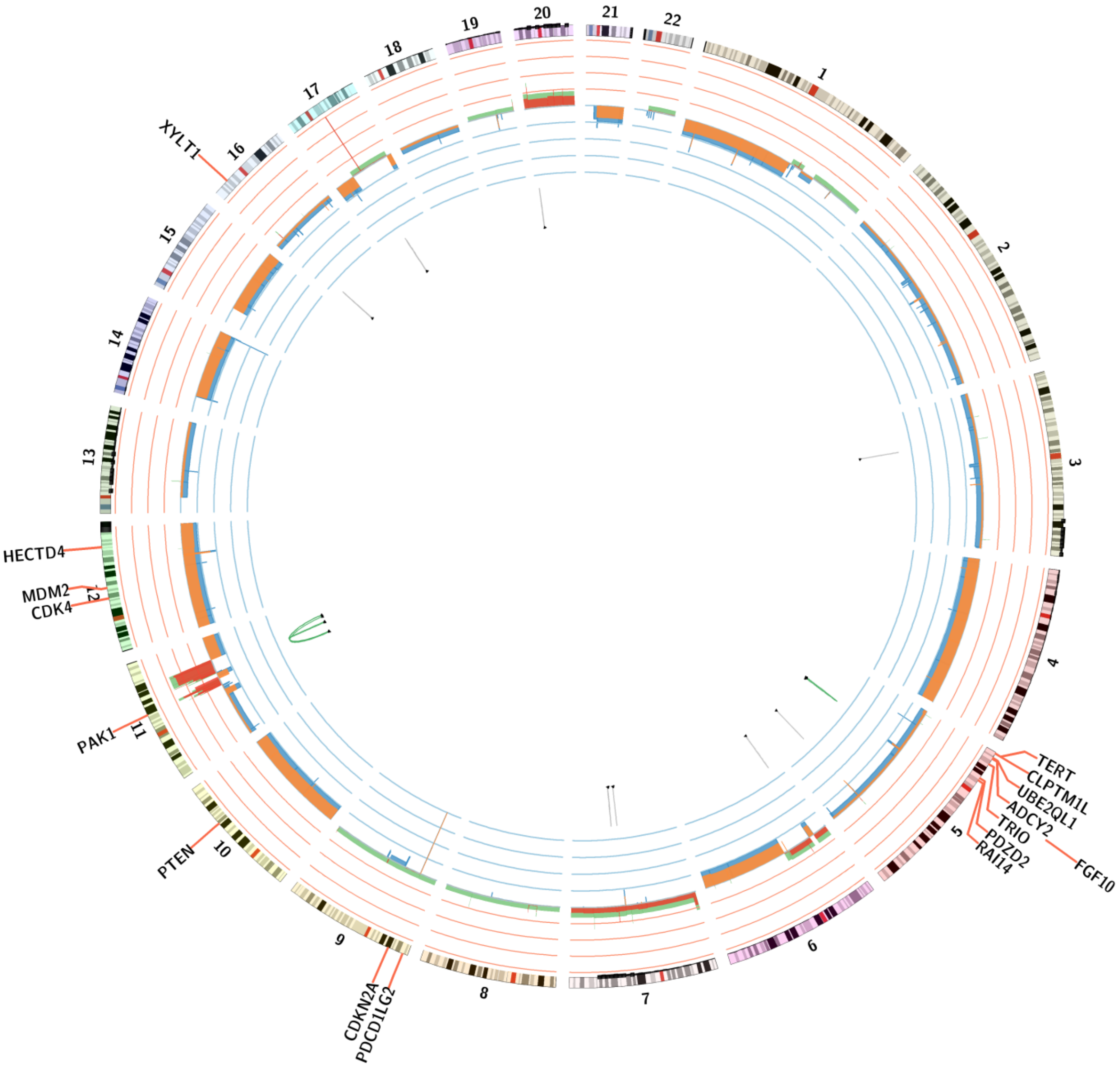

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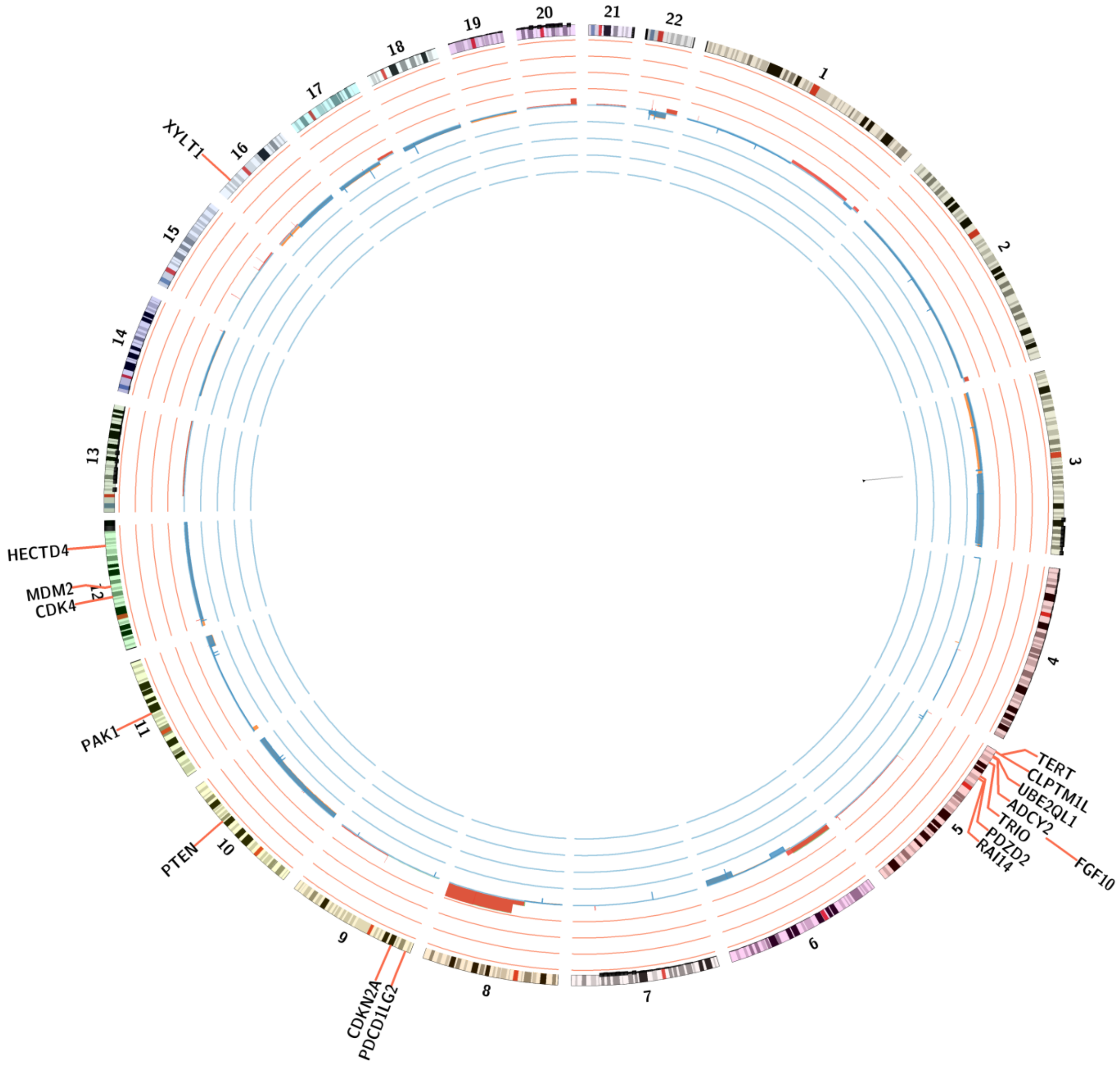
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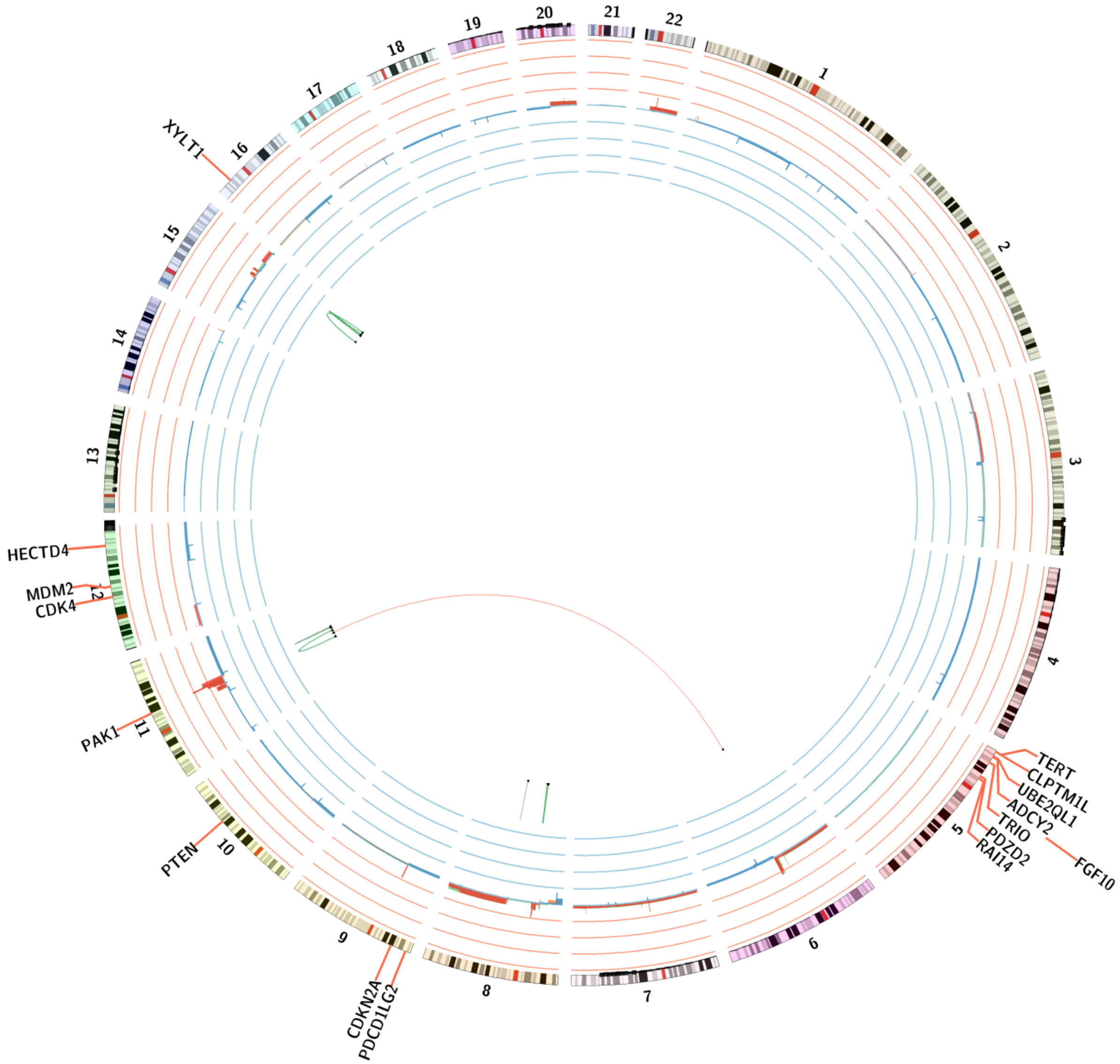
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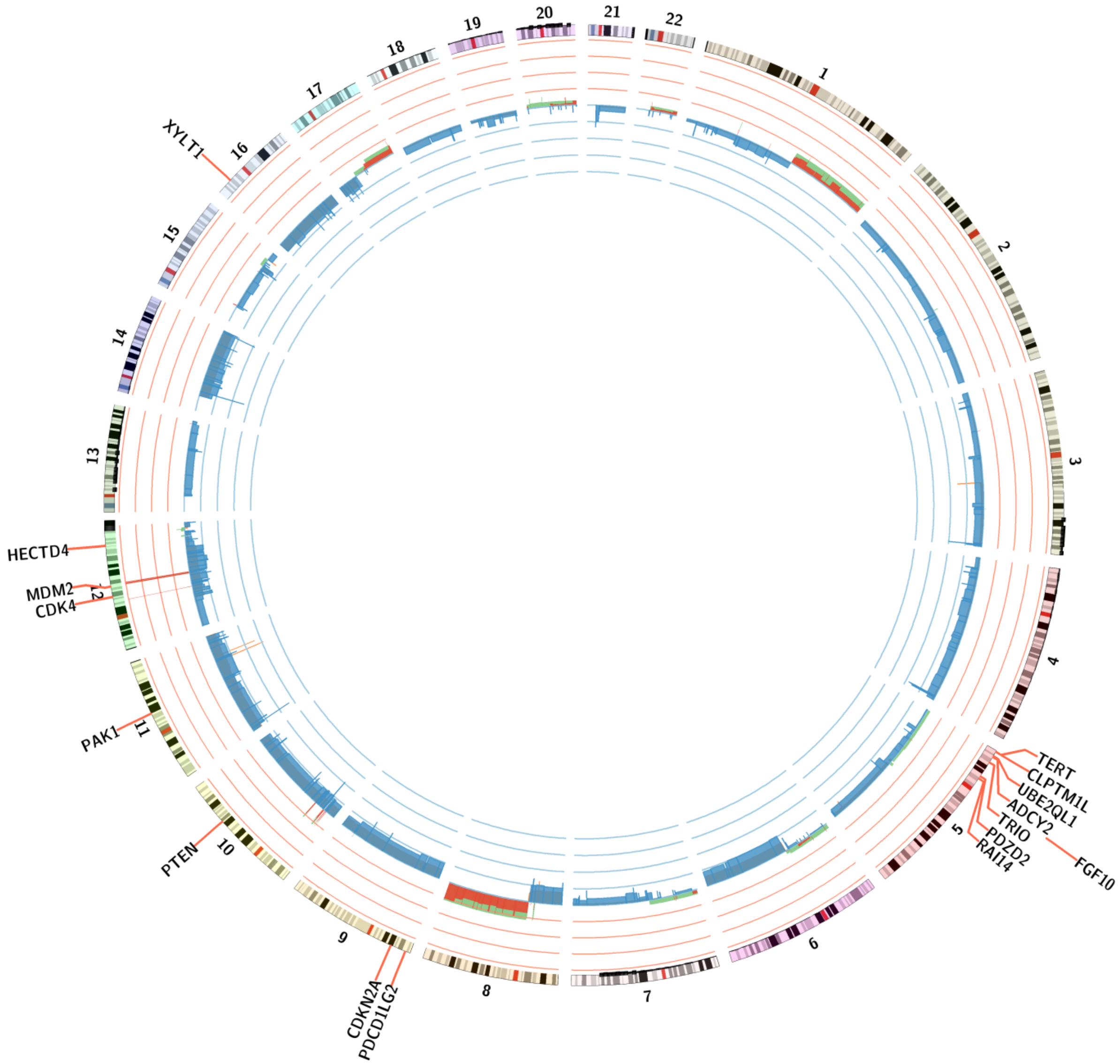
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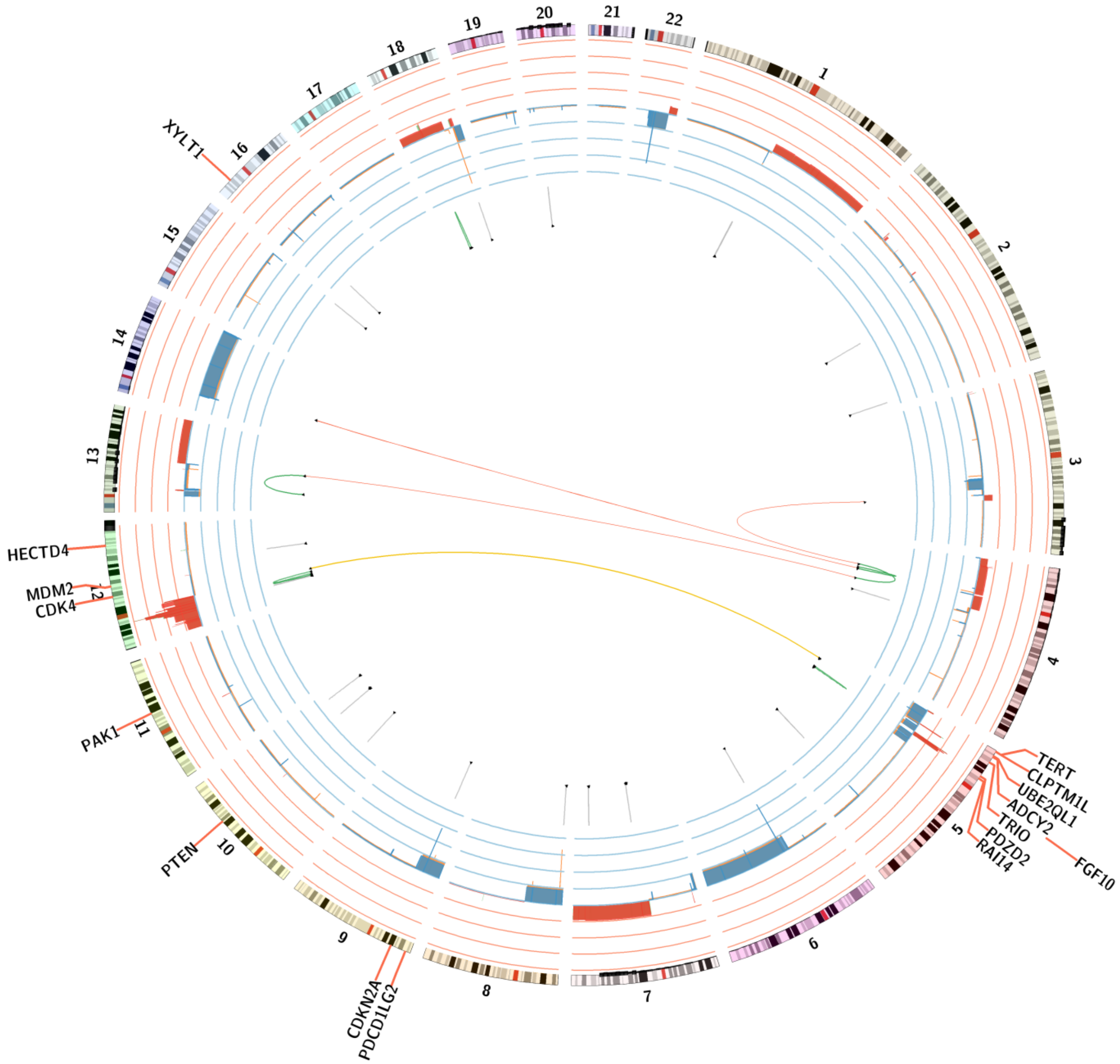

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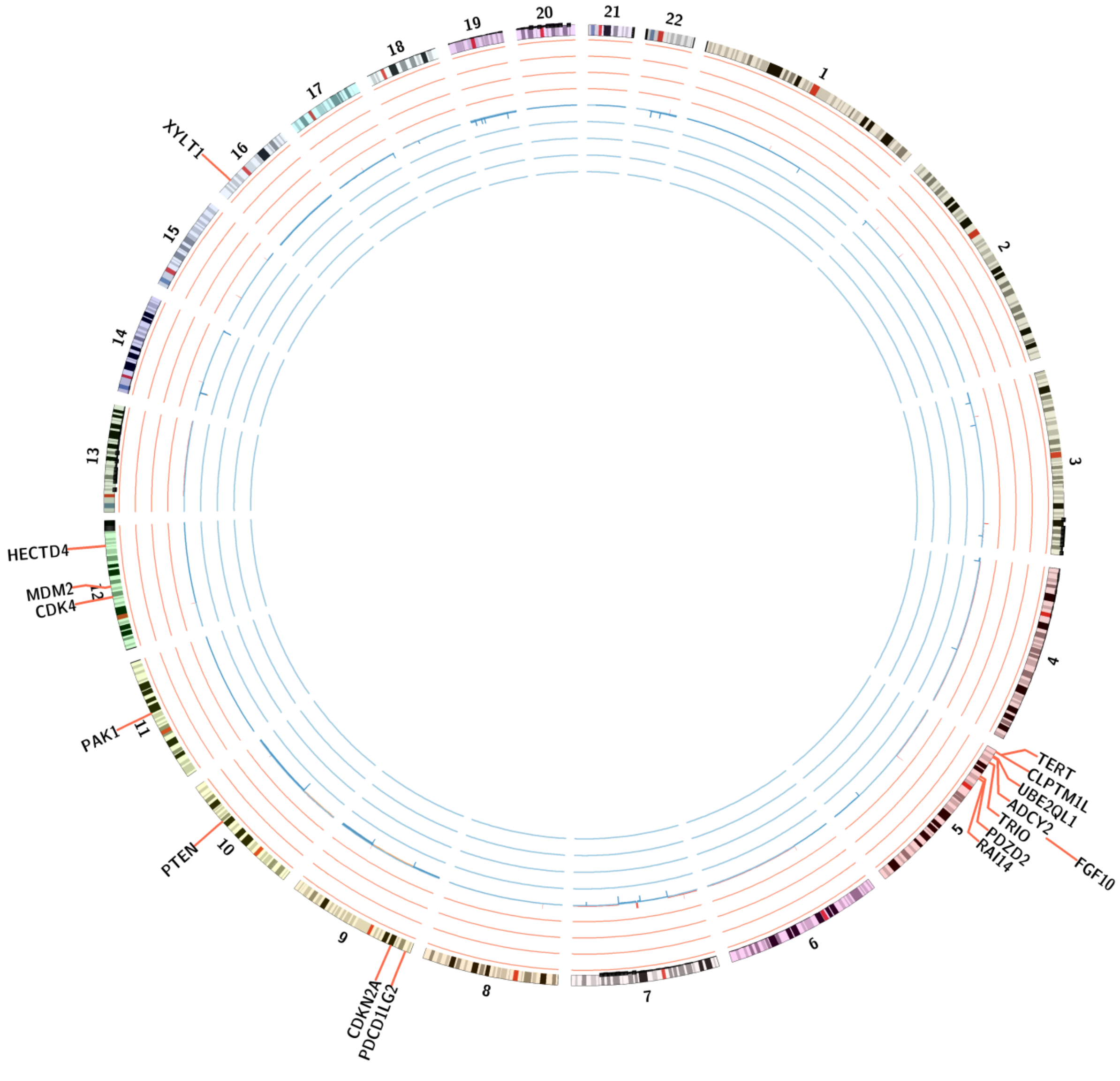
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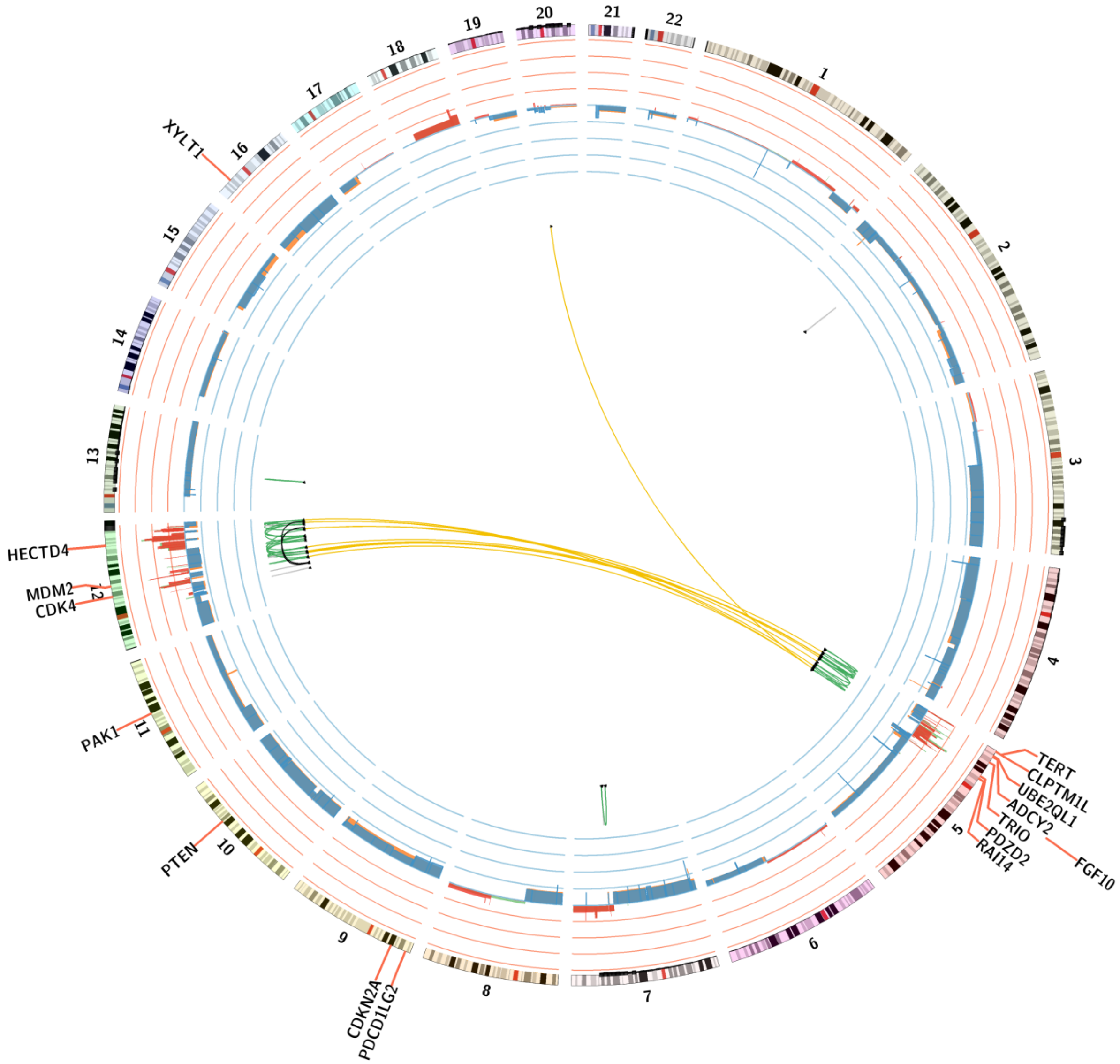
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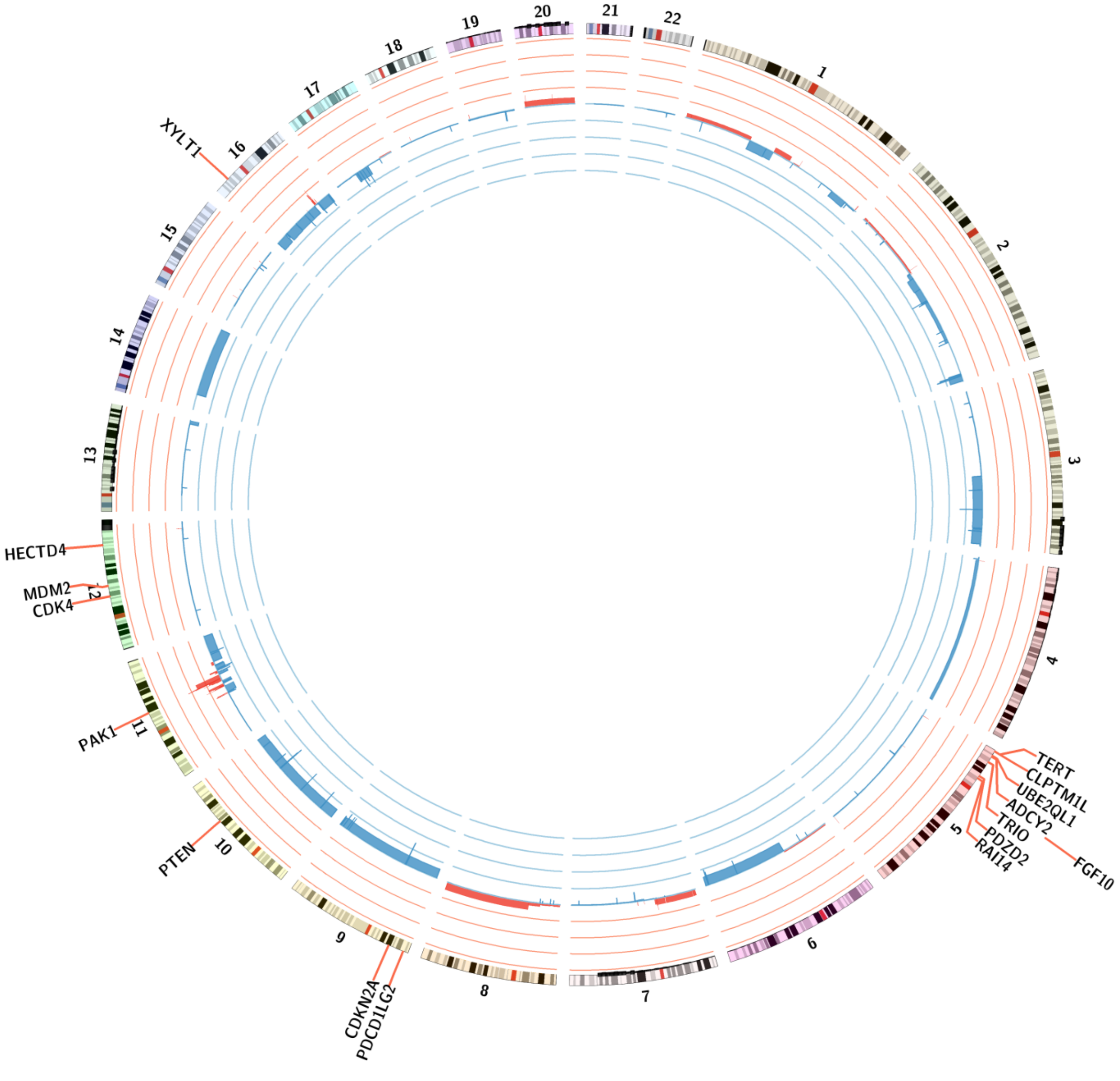
Patient 8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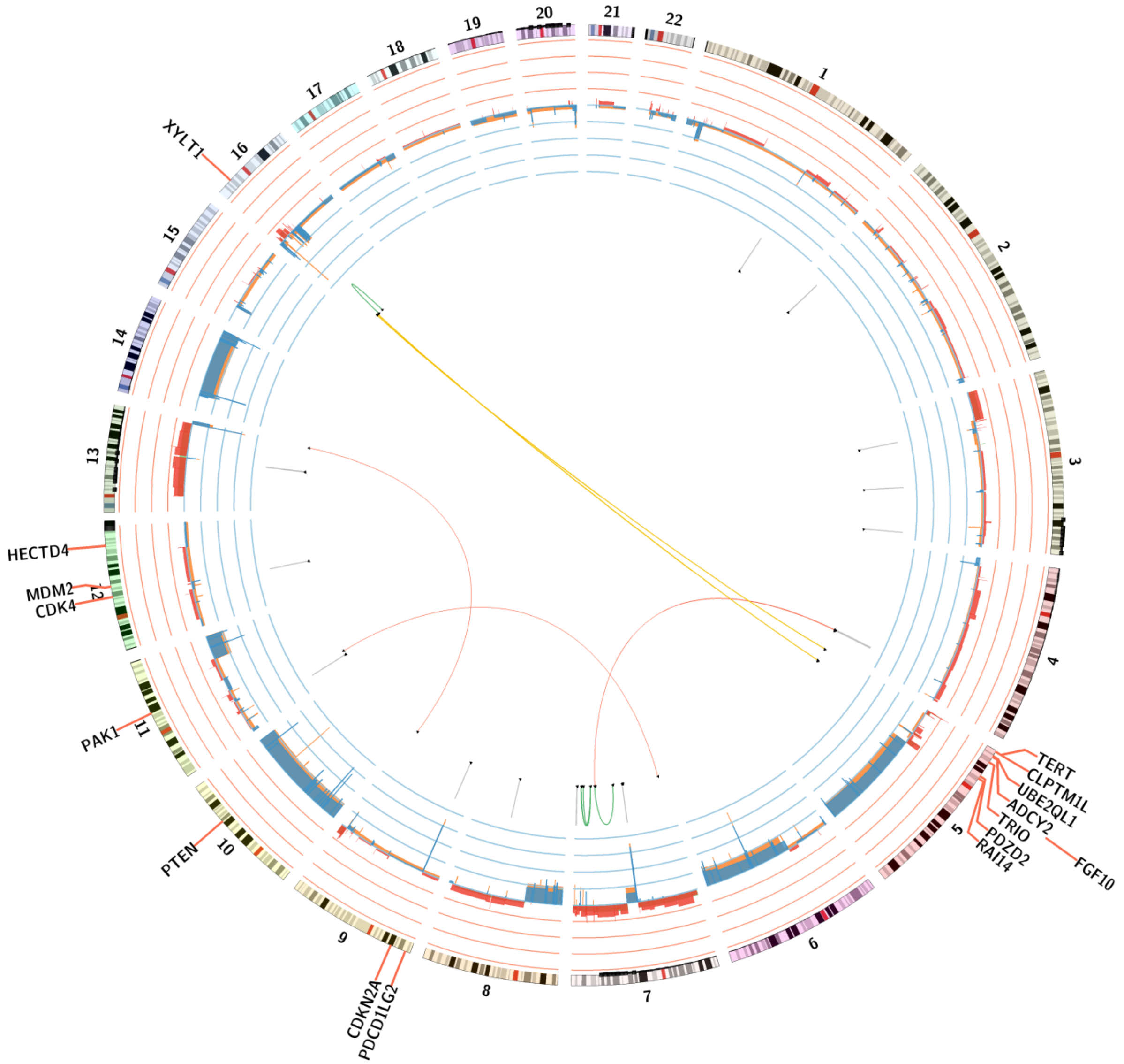

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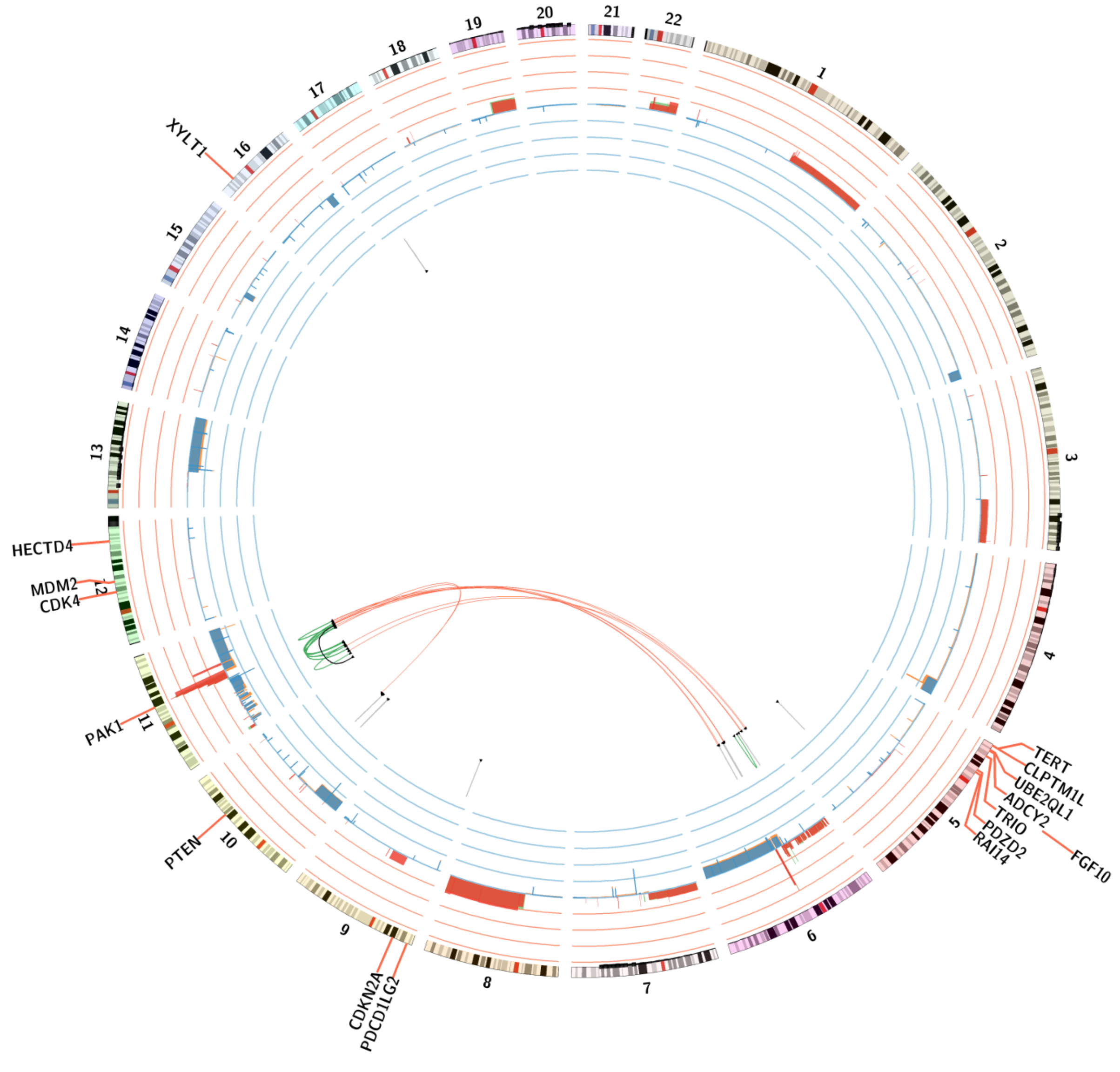
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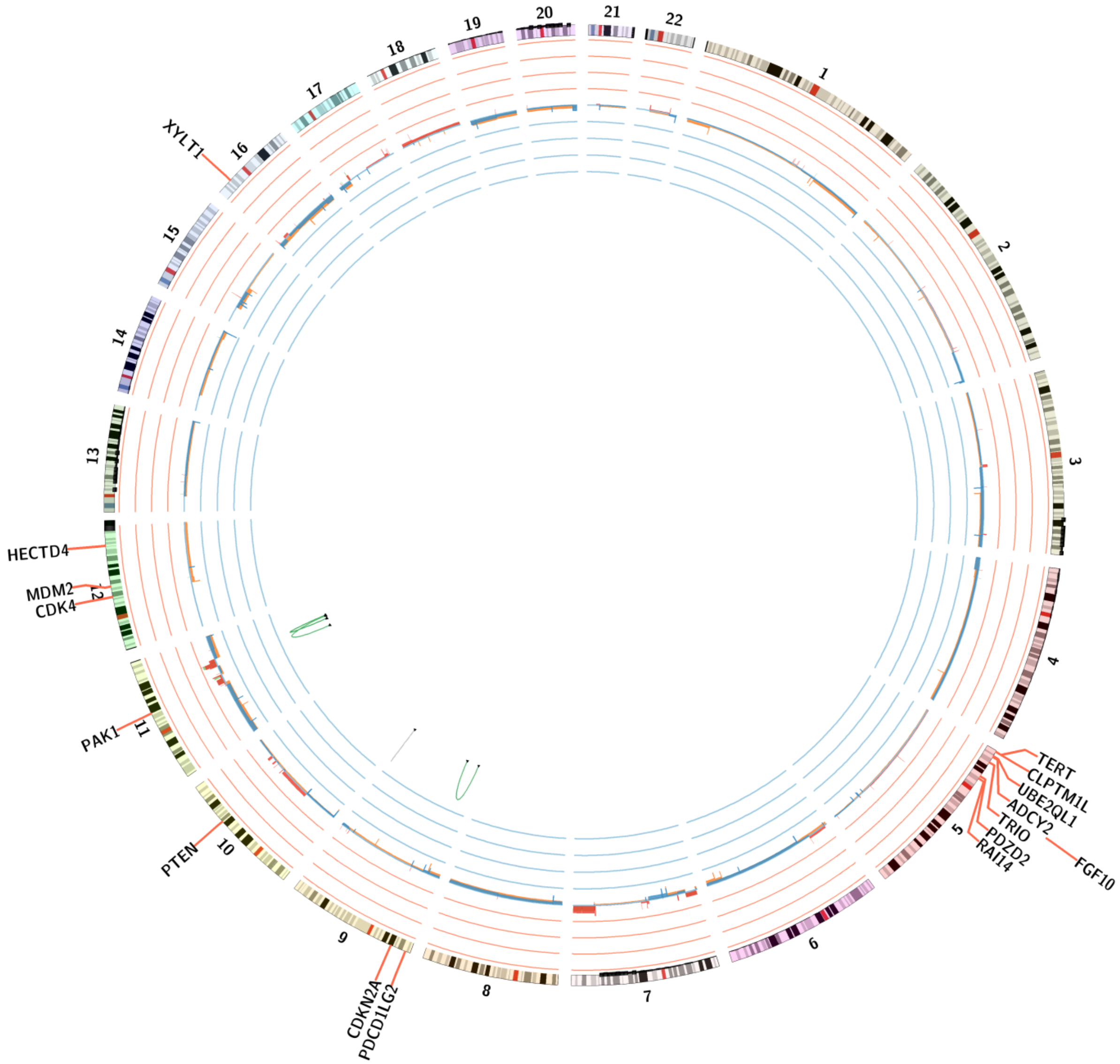
Patient 11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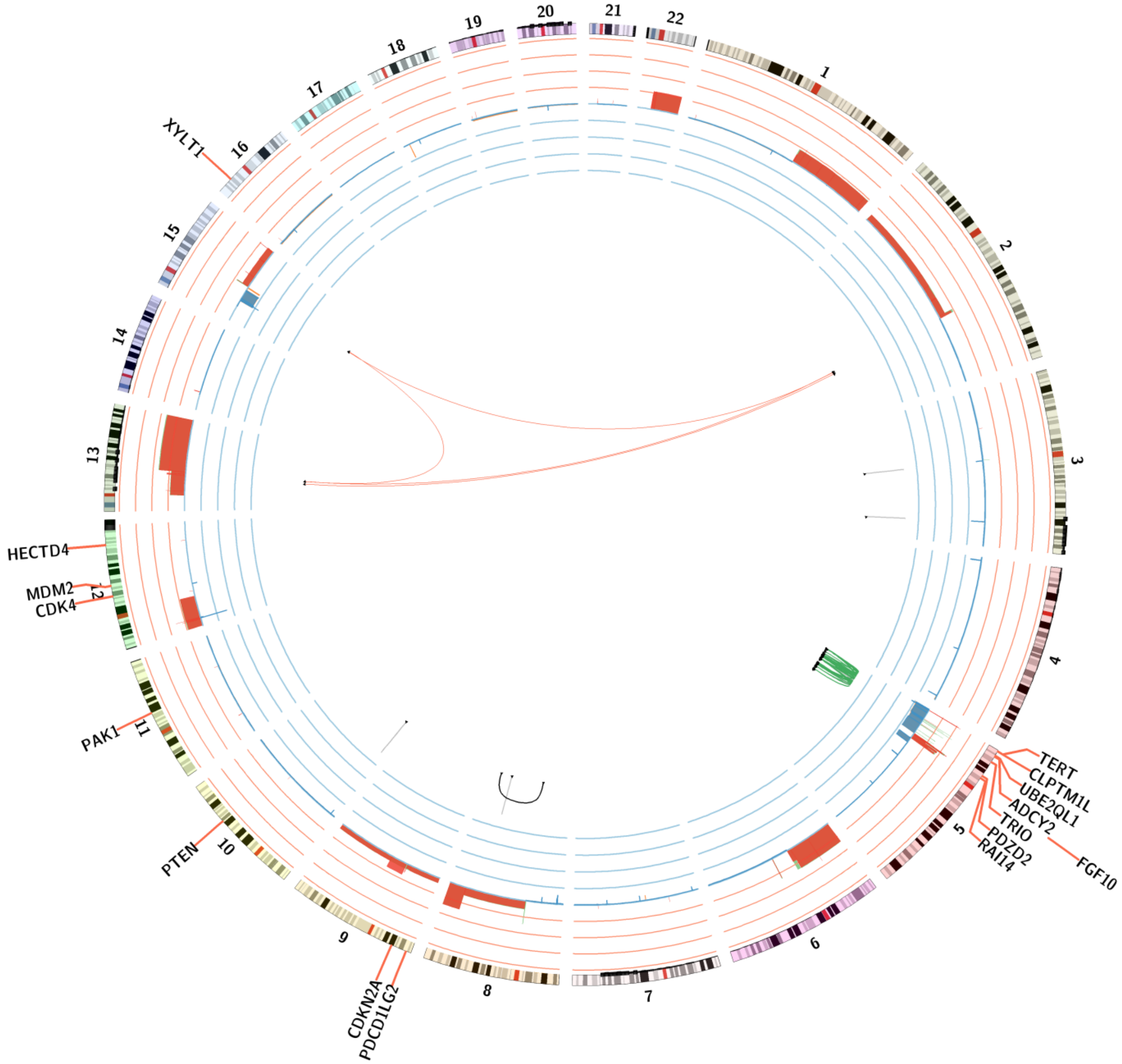
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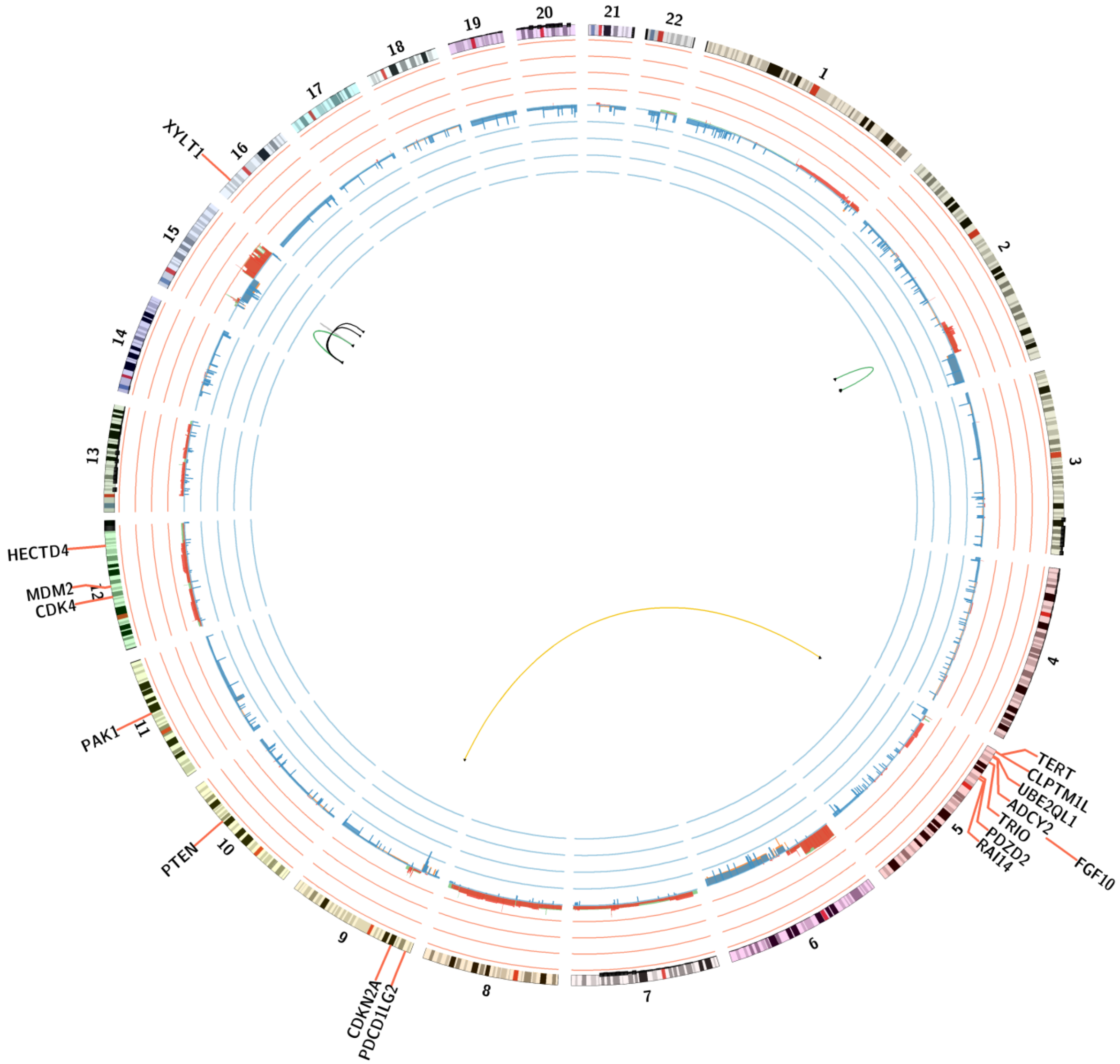
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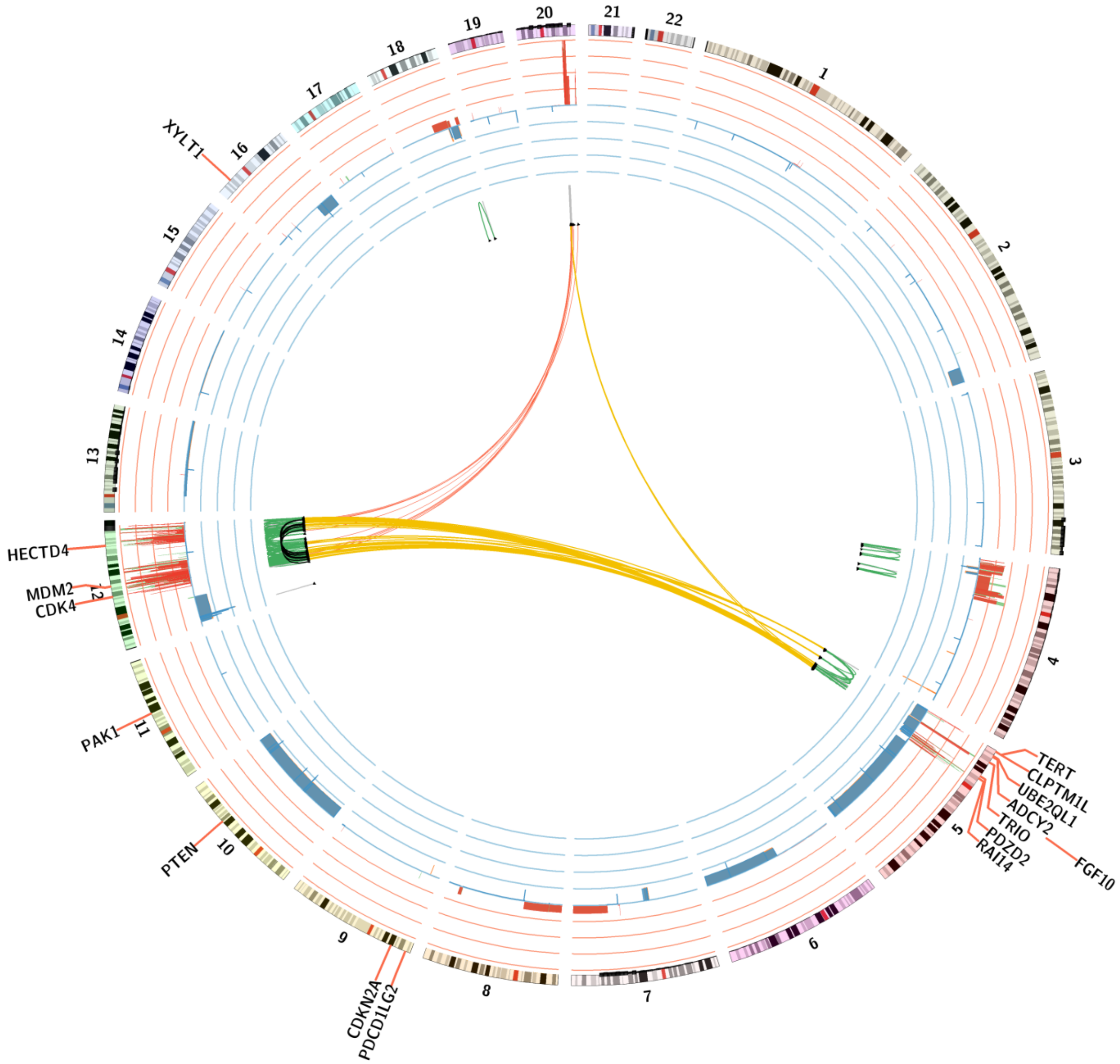
Patient 14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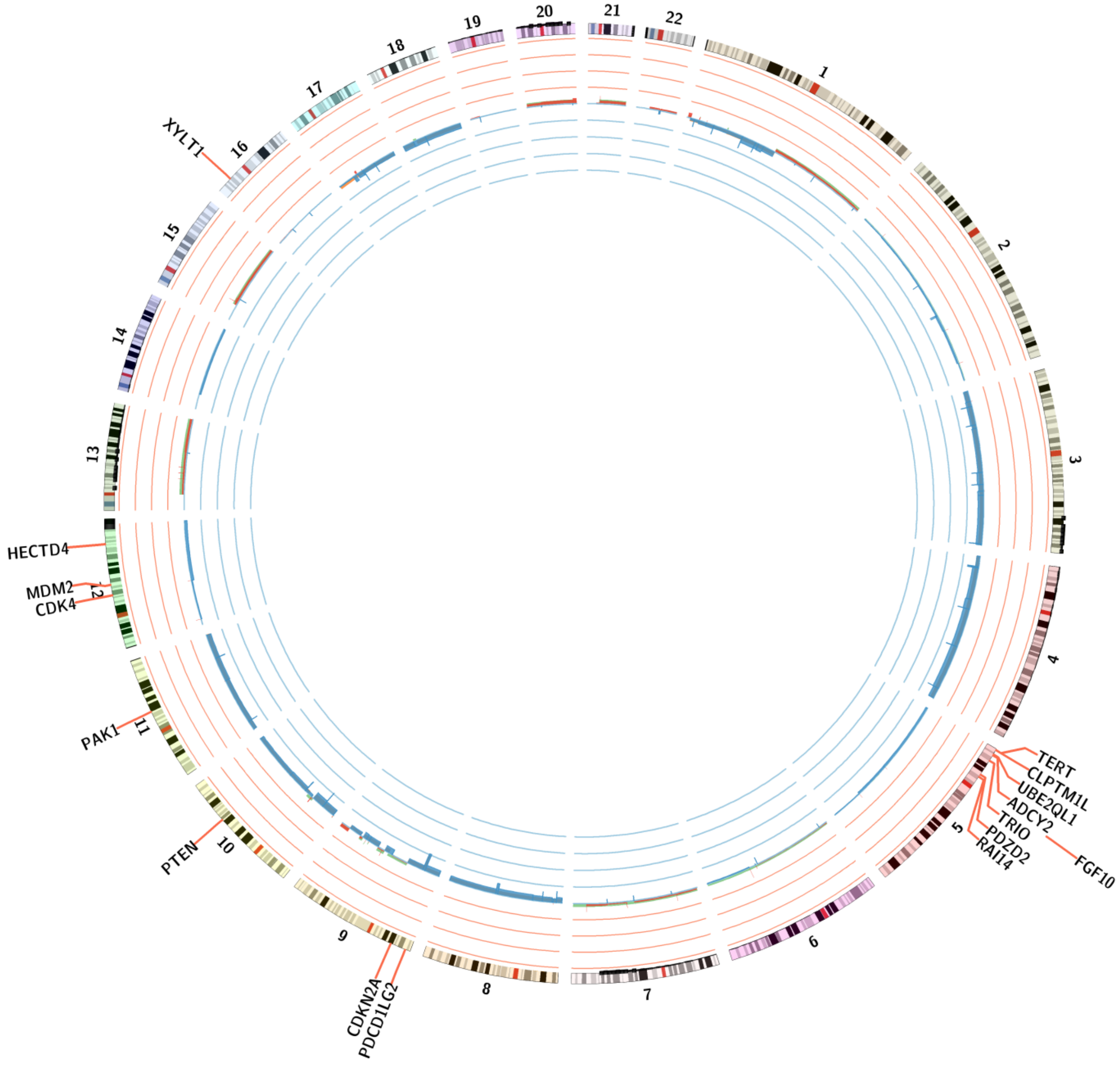
Patient 15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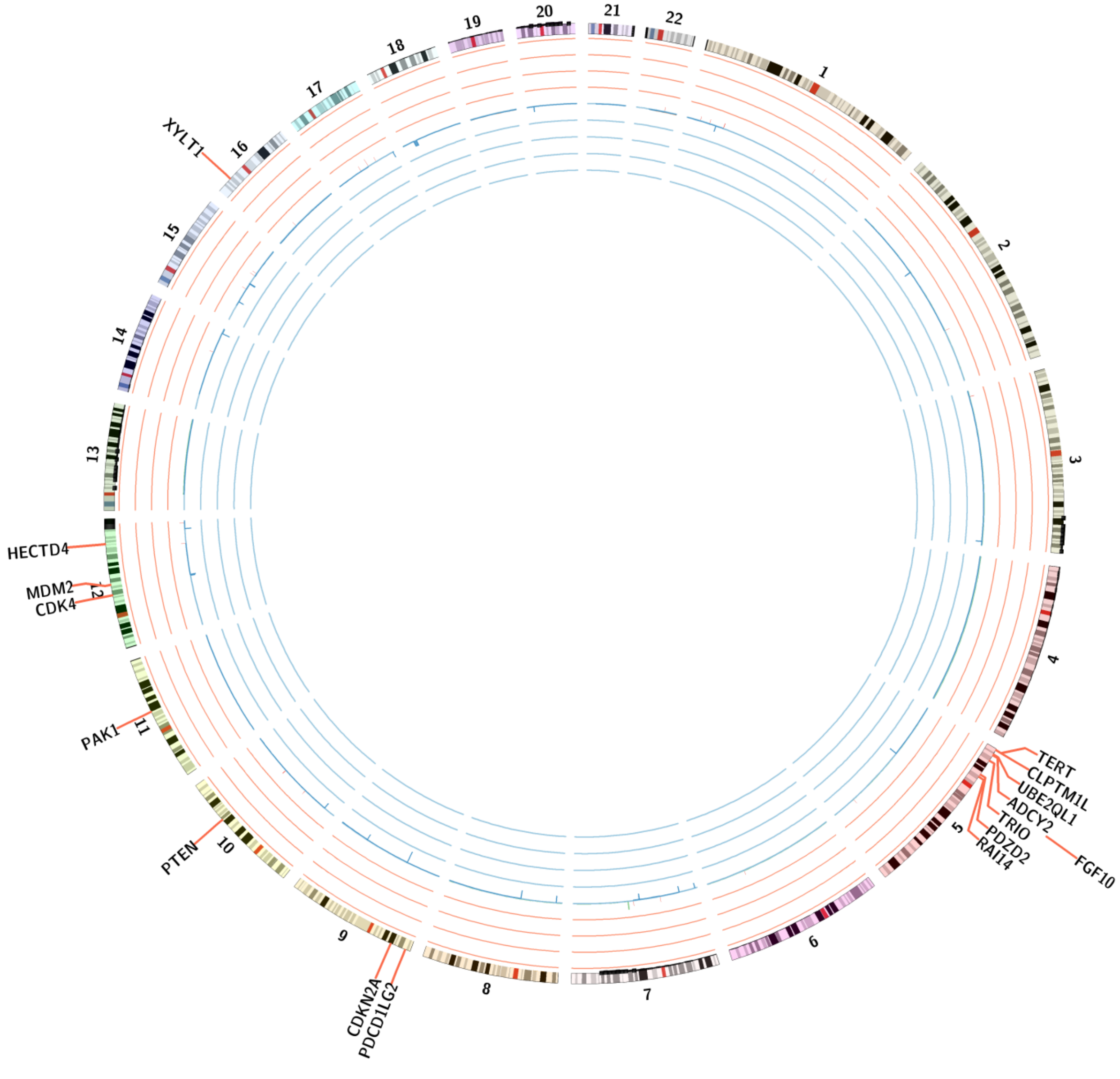
Patient 16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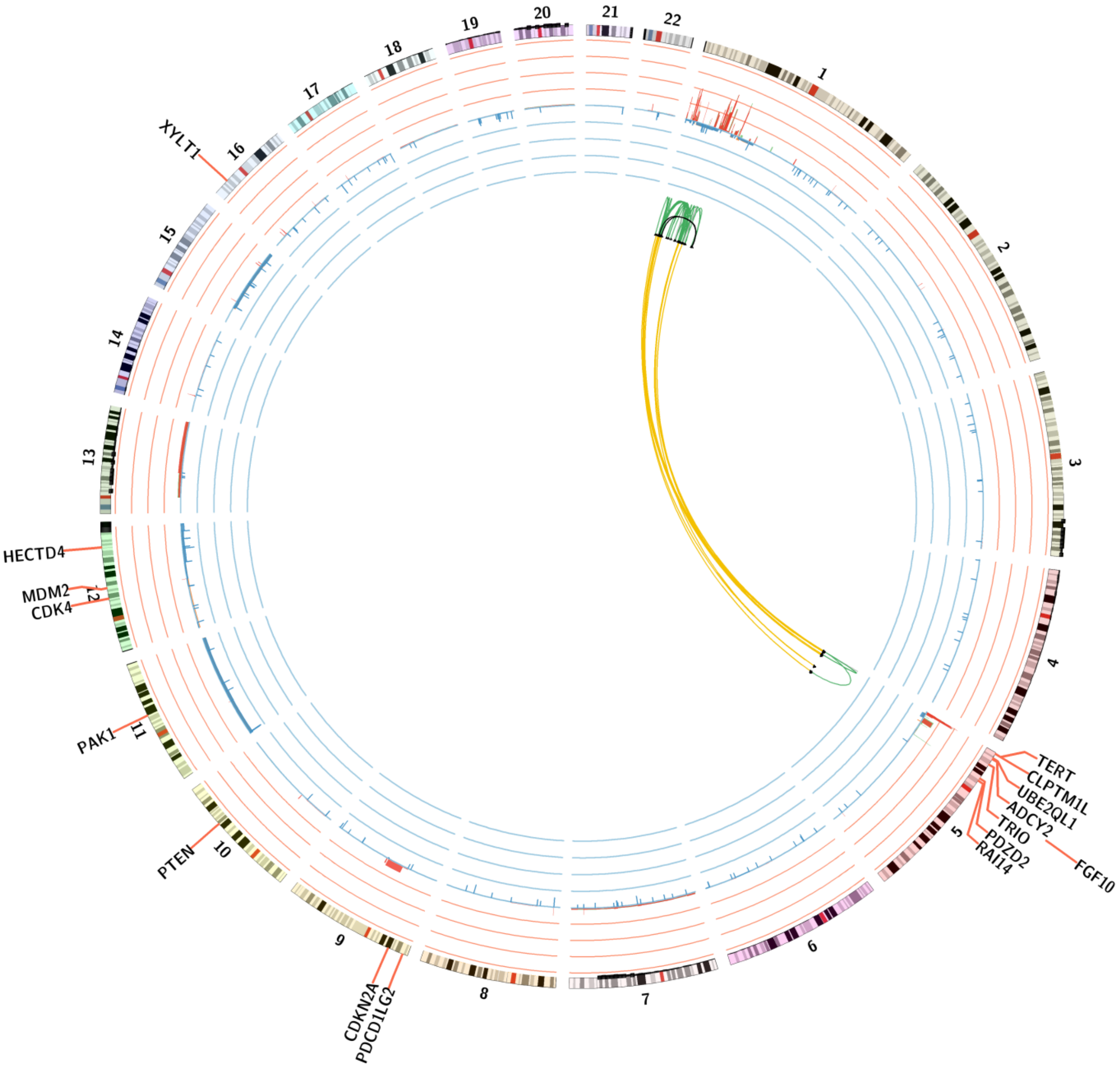
Patient 17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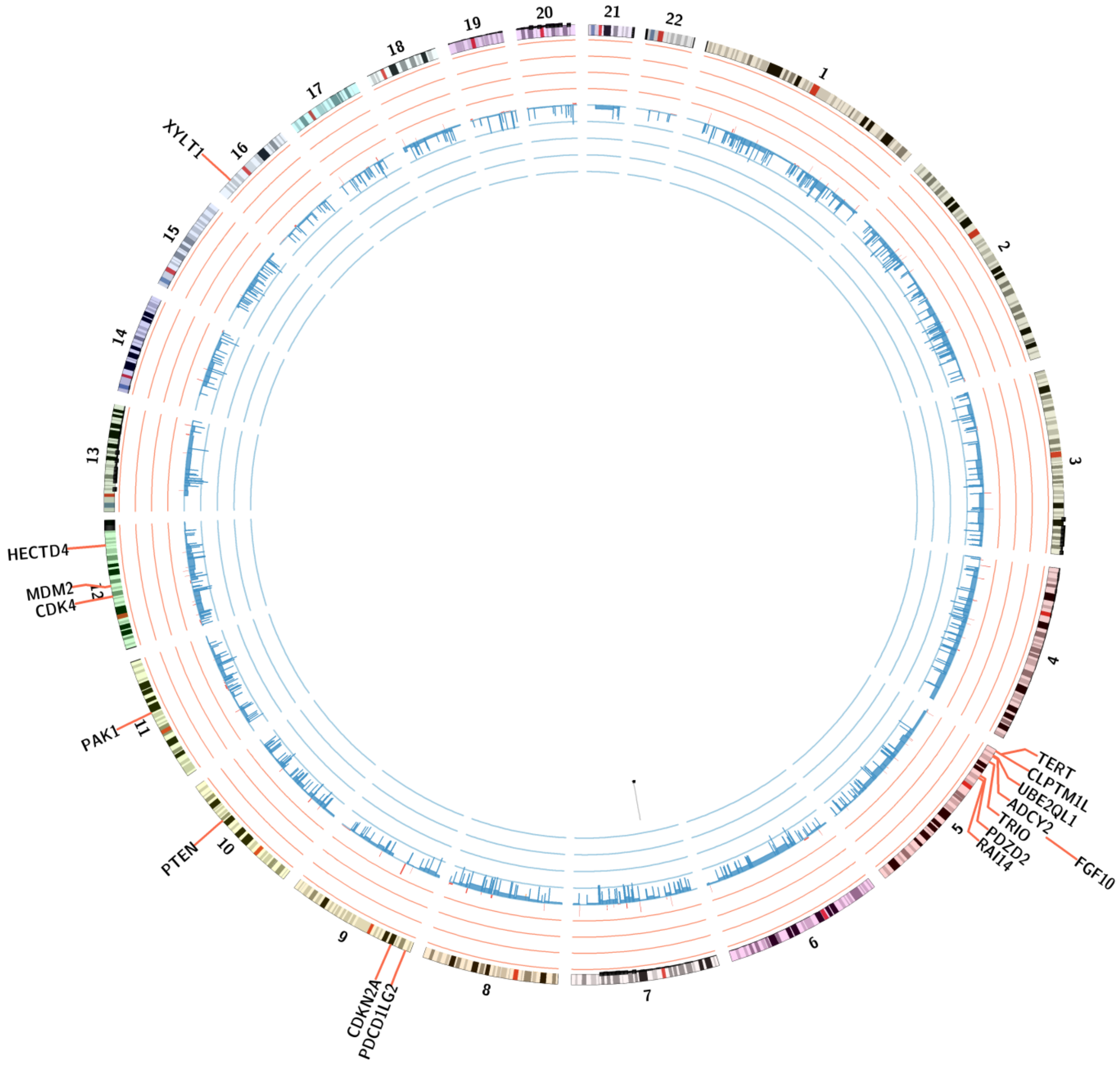

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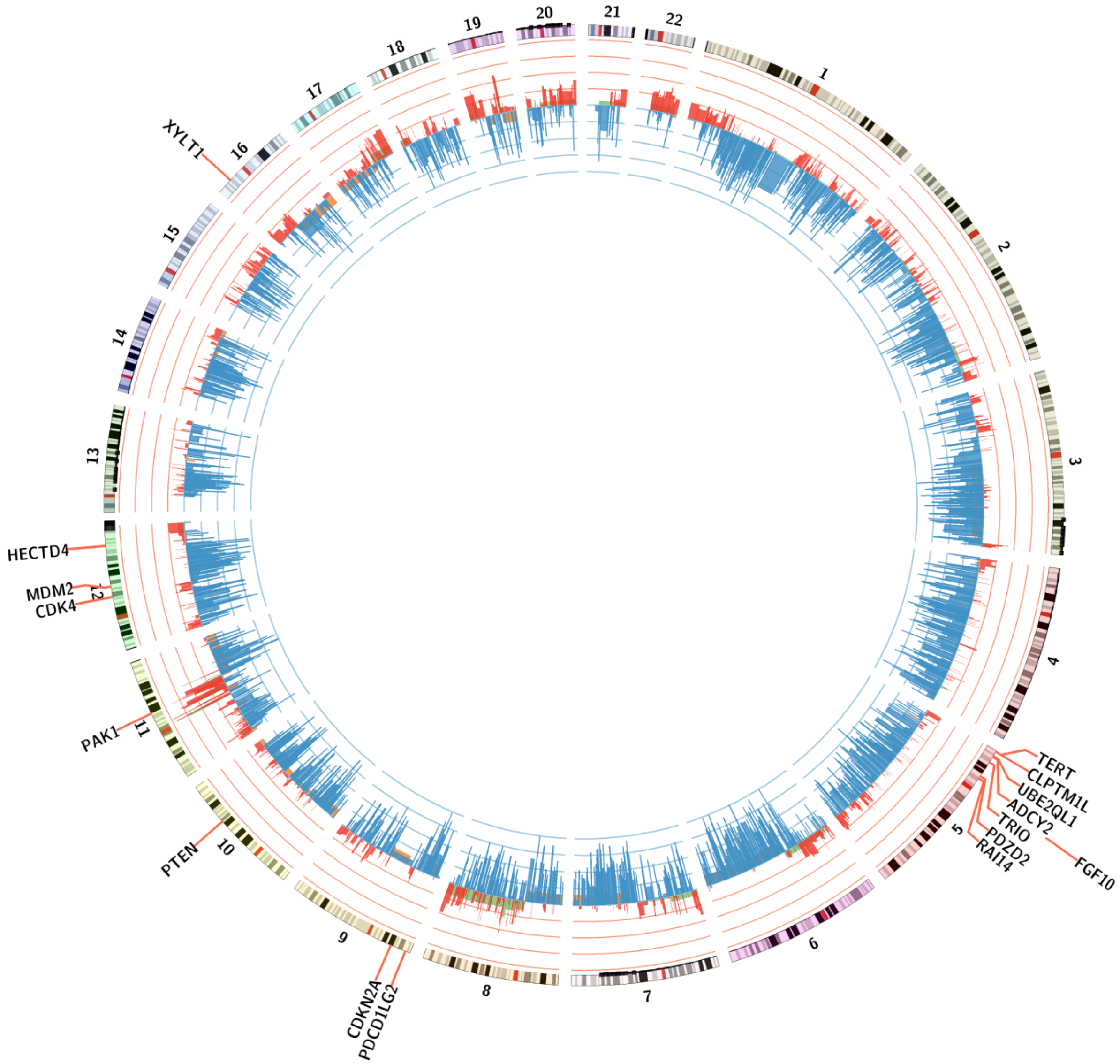
Patient 19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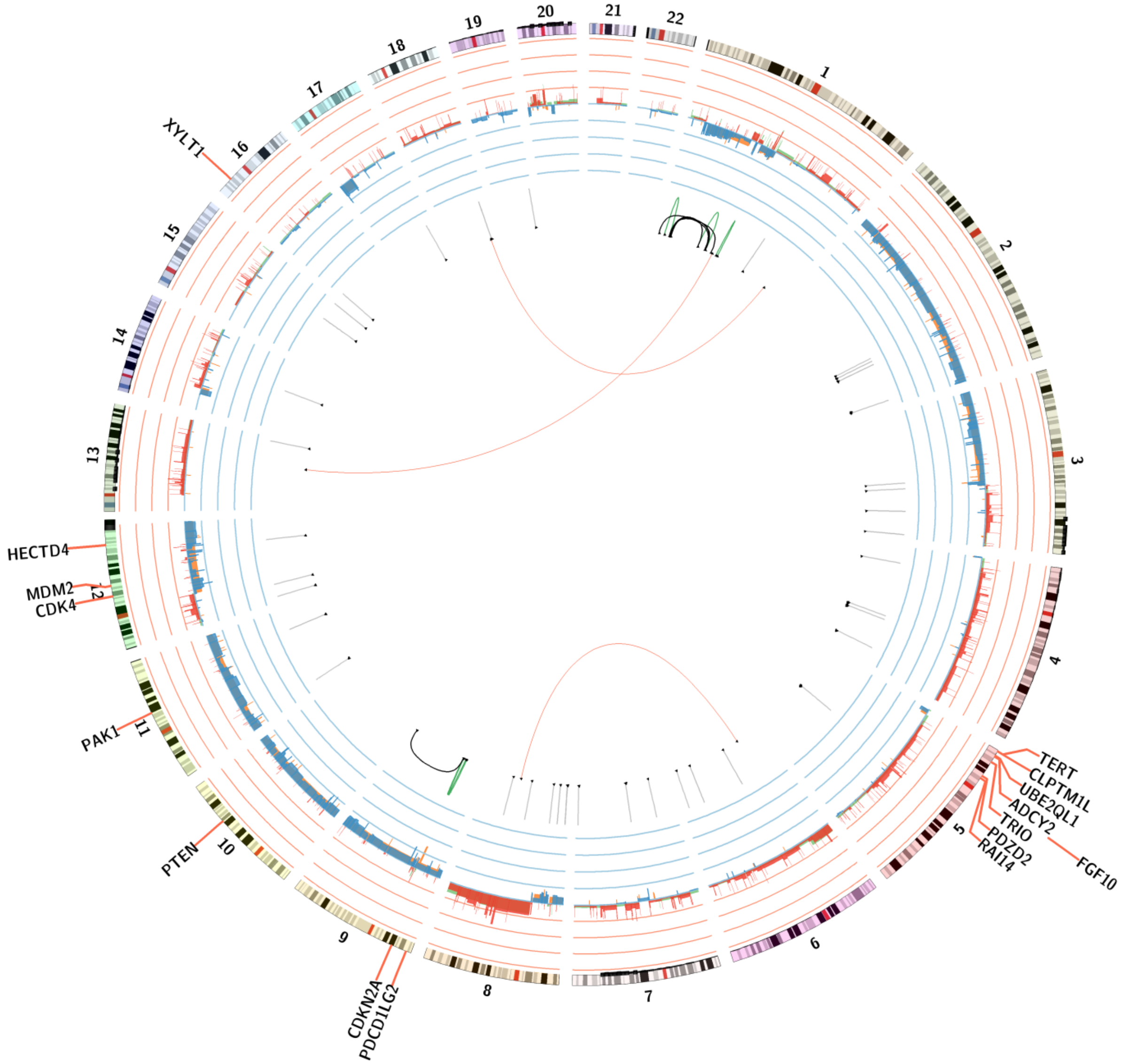
Patient 20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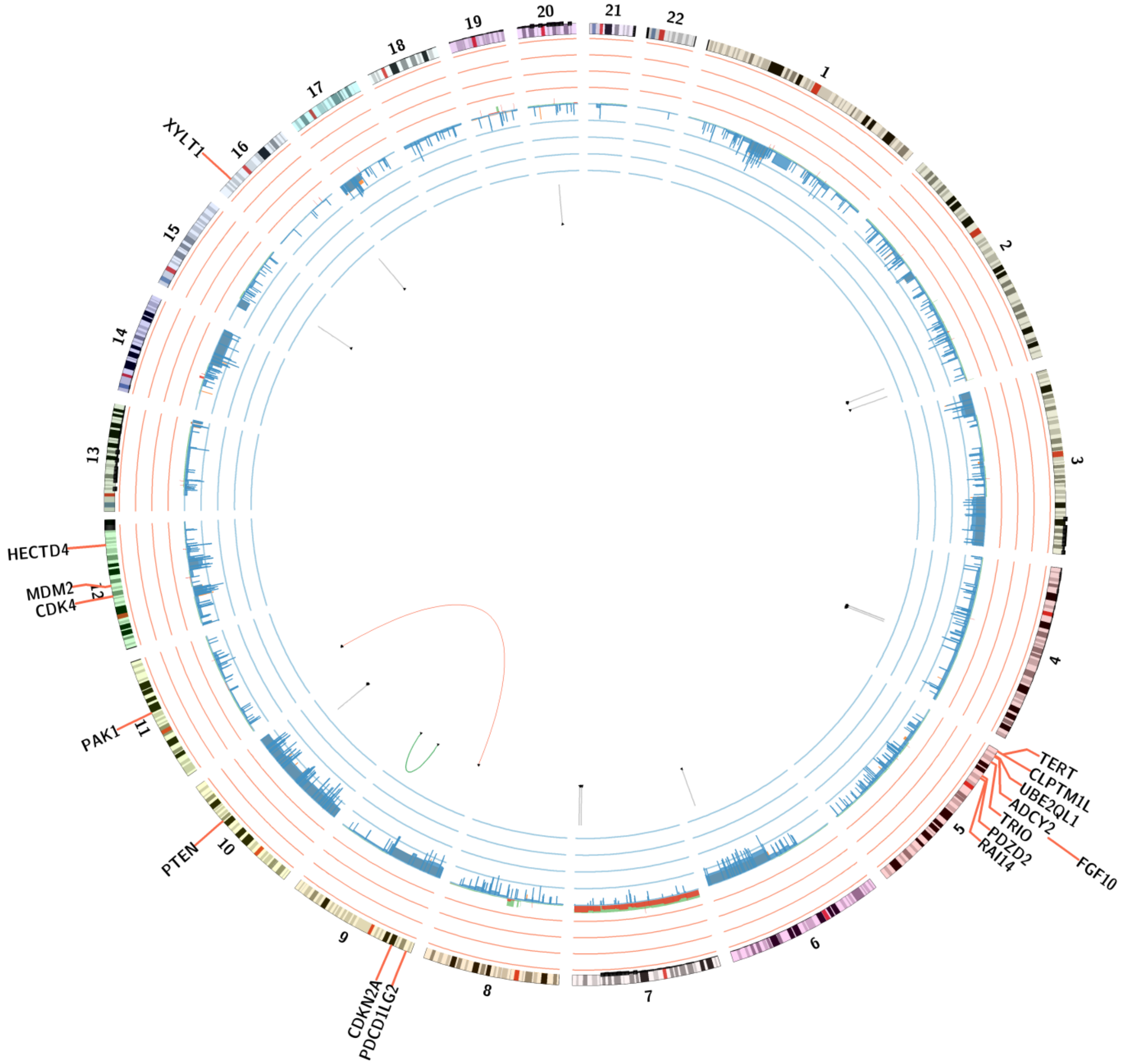
Patient 21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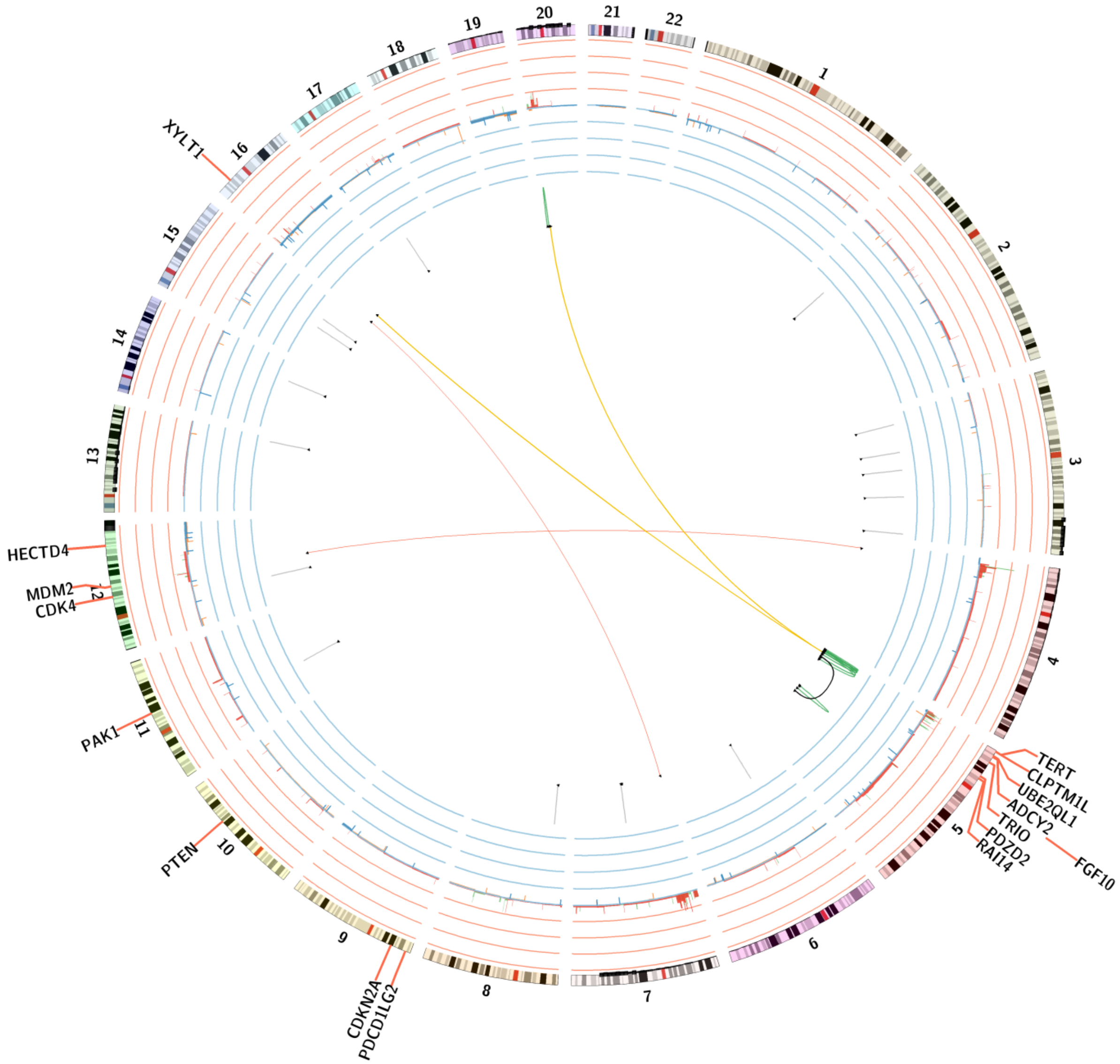
Patient 22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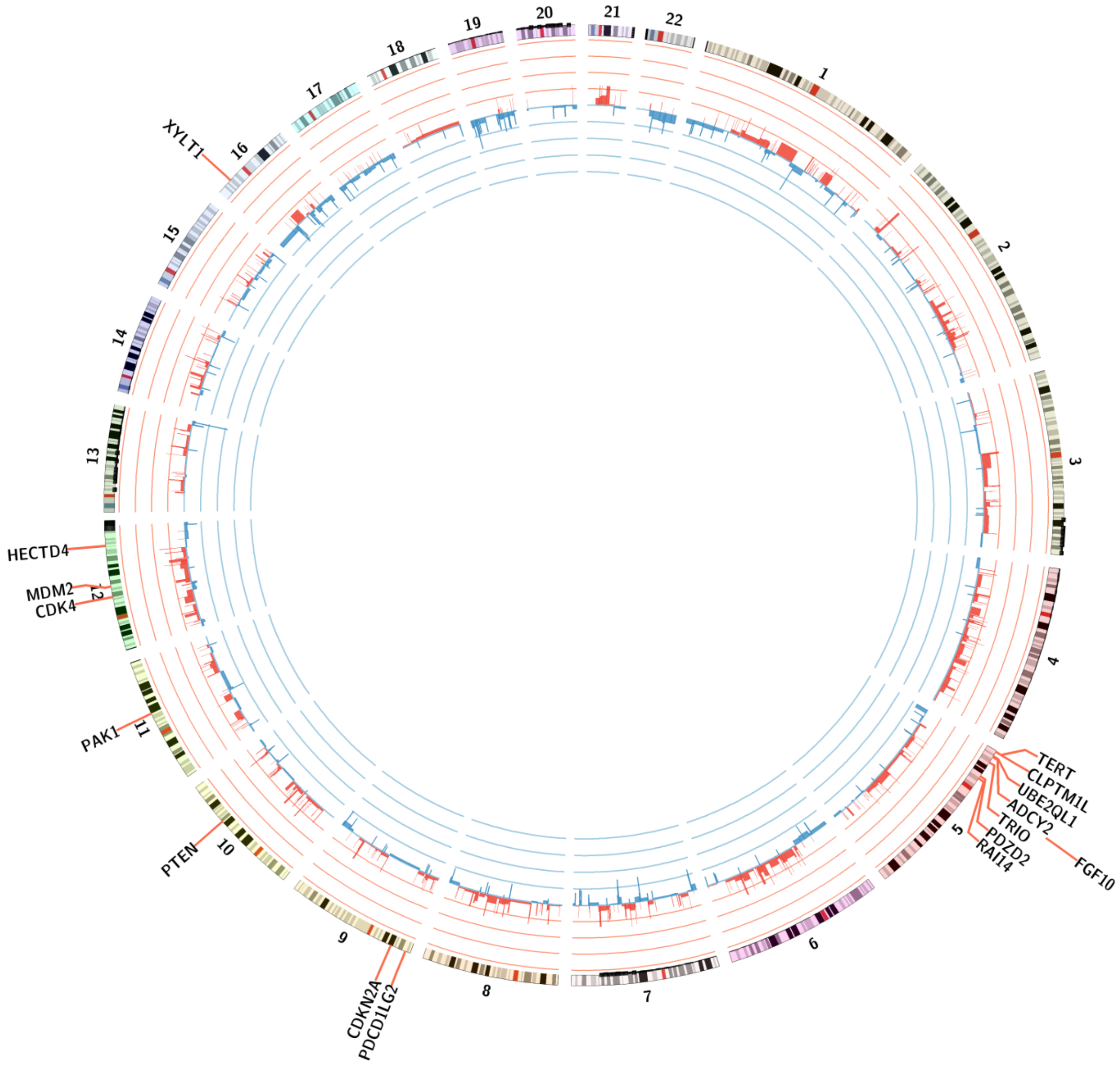
Patient 23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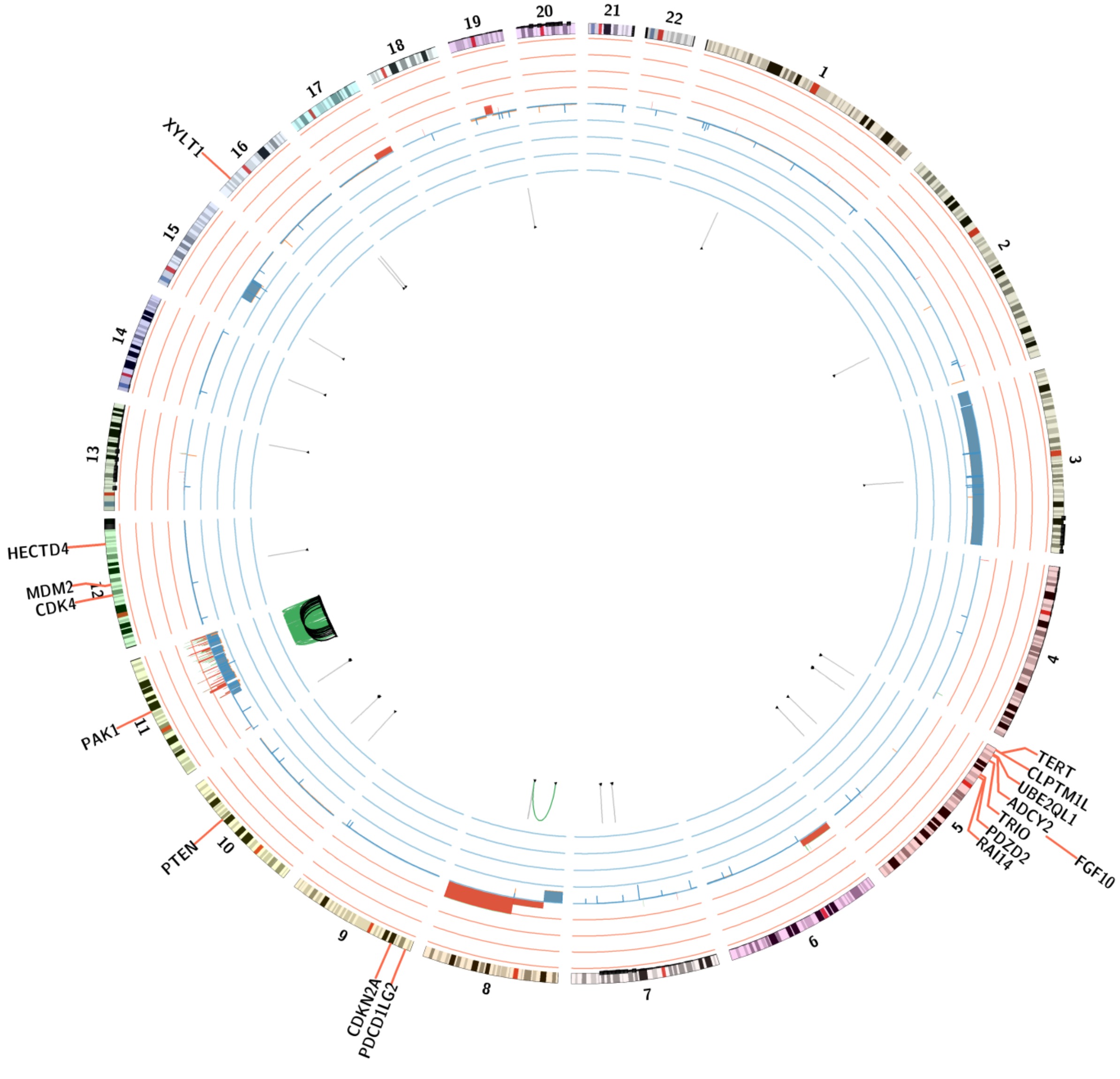
Patient 24



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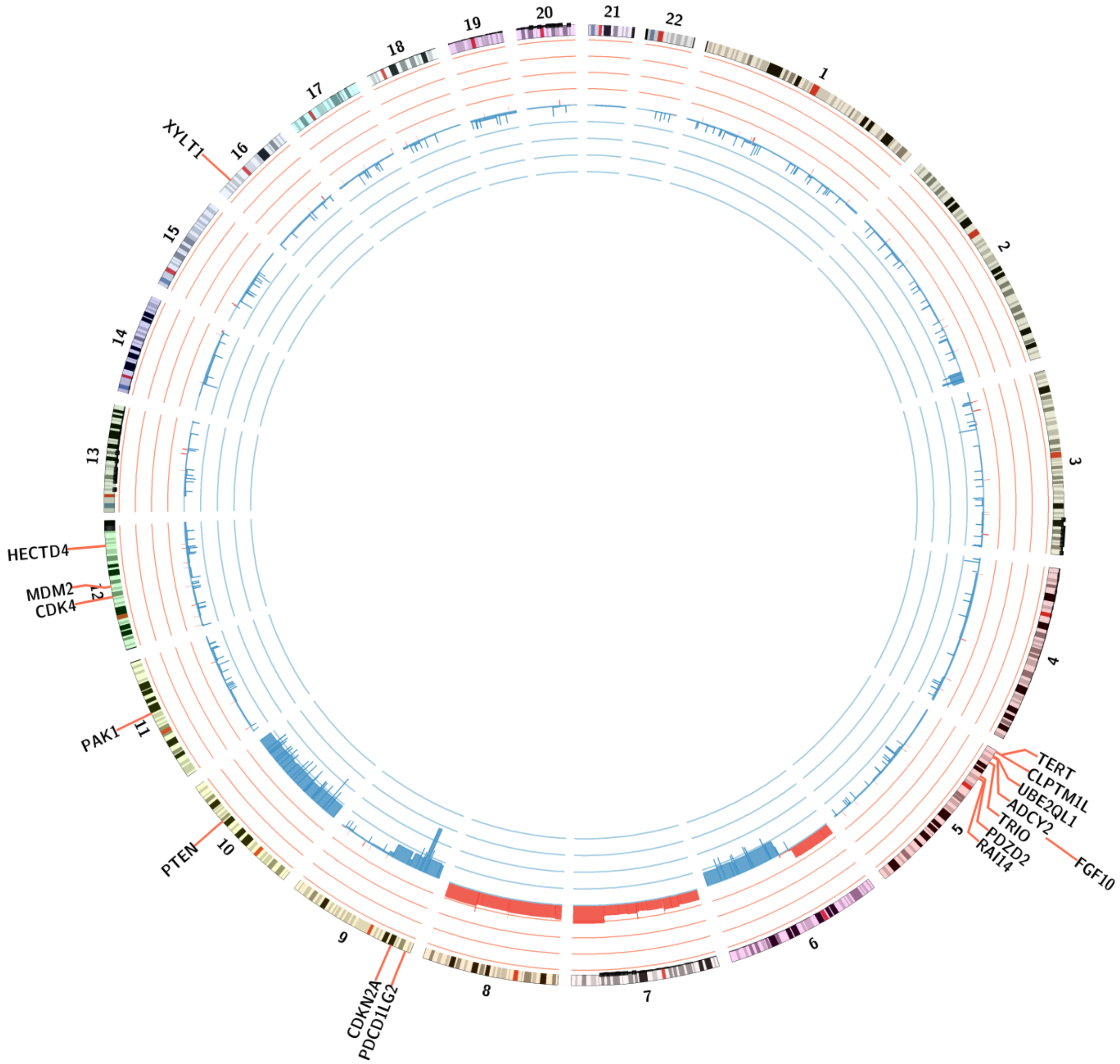
Patient 25 (sample 25a)



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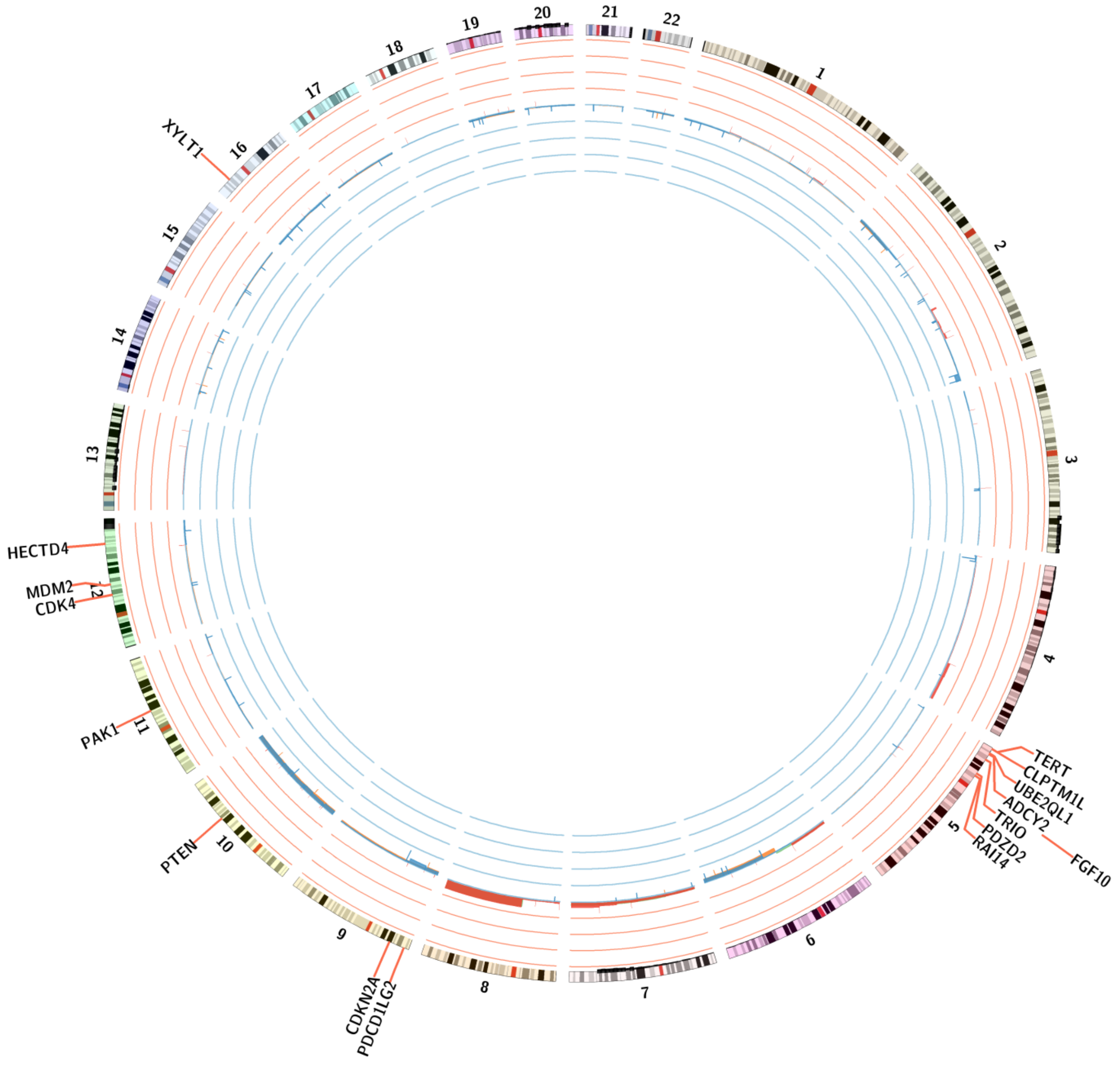
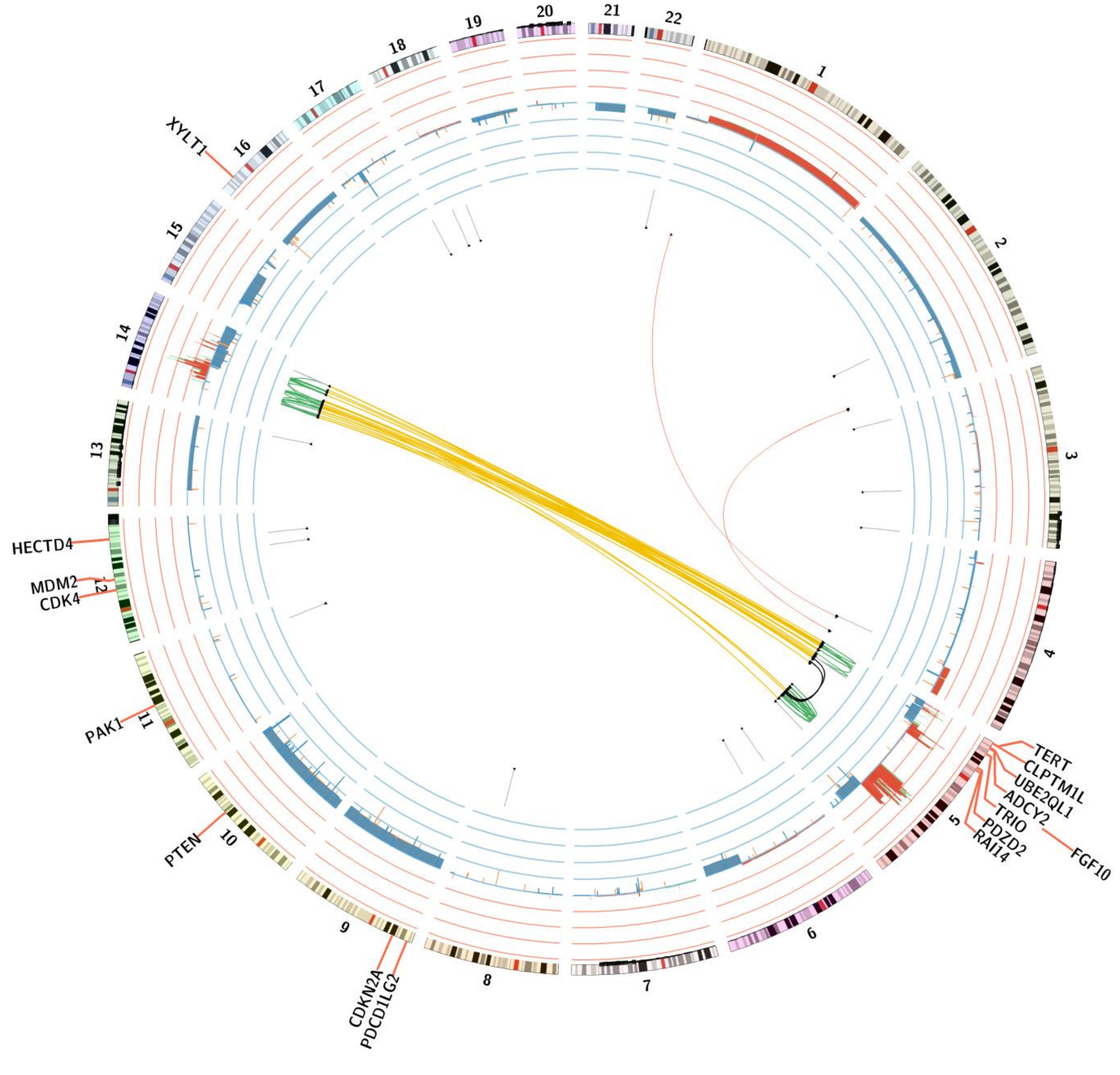


Patient 26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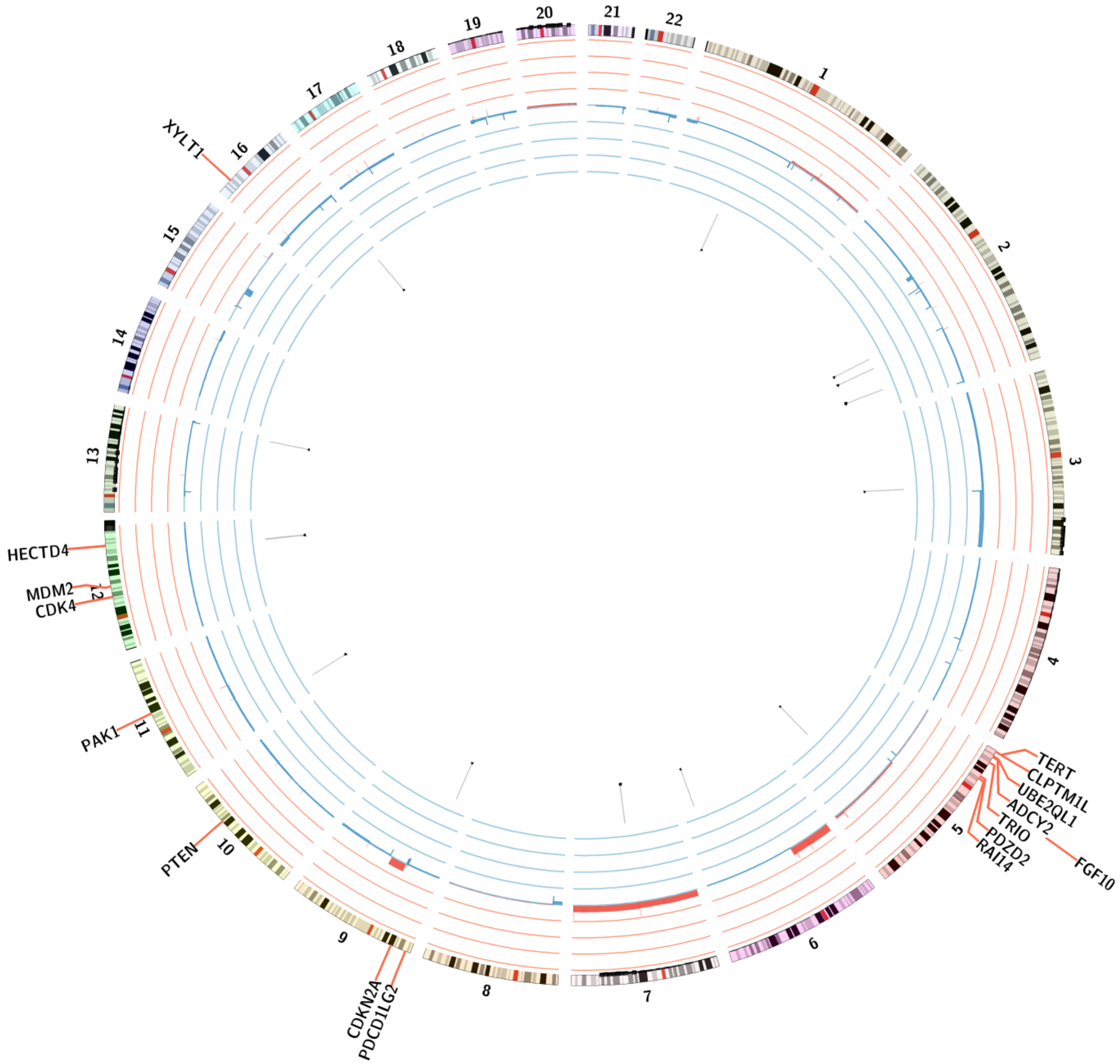
Patient 27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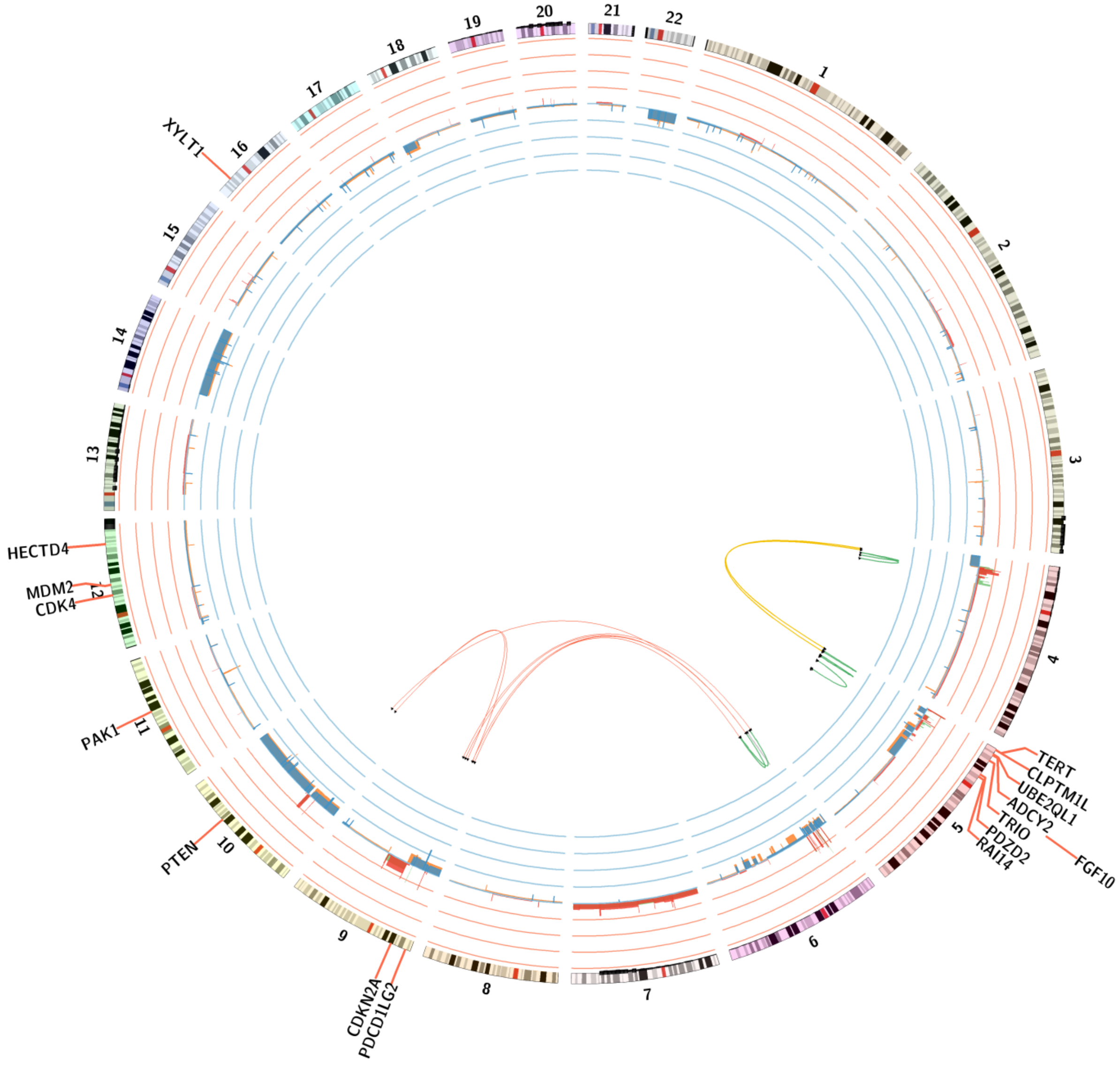
Patient 28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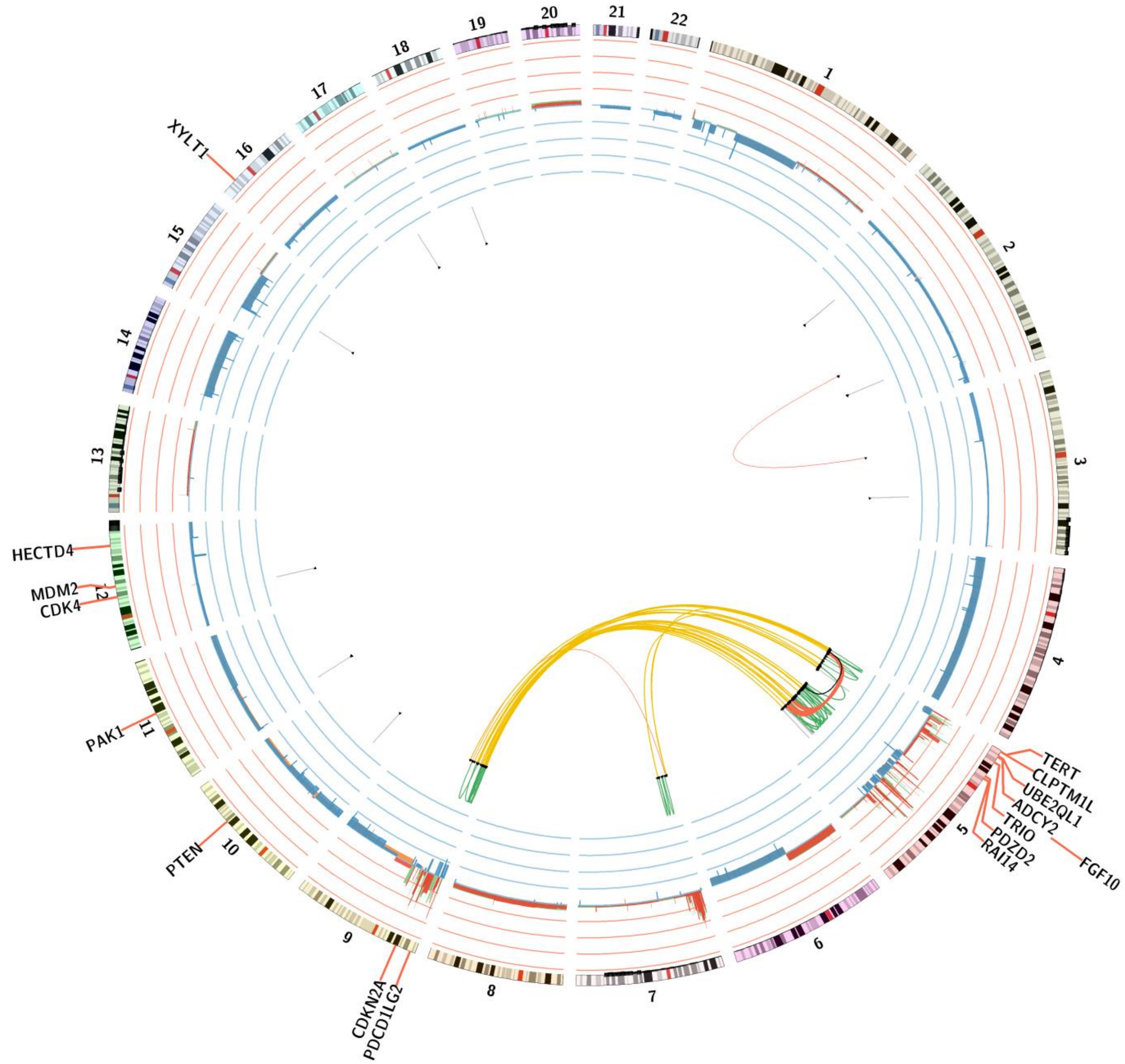
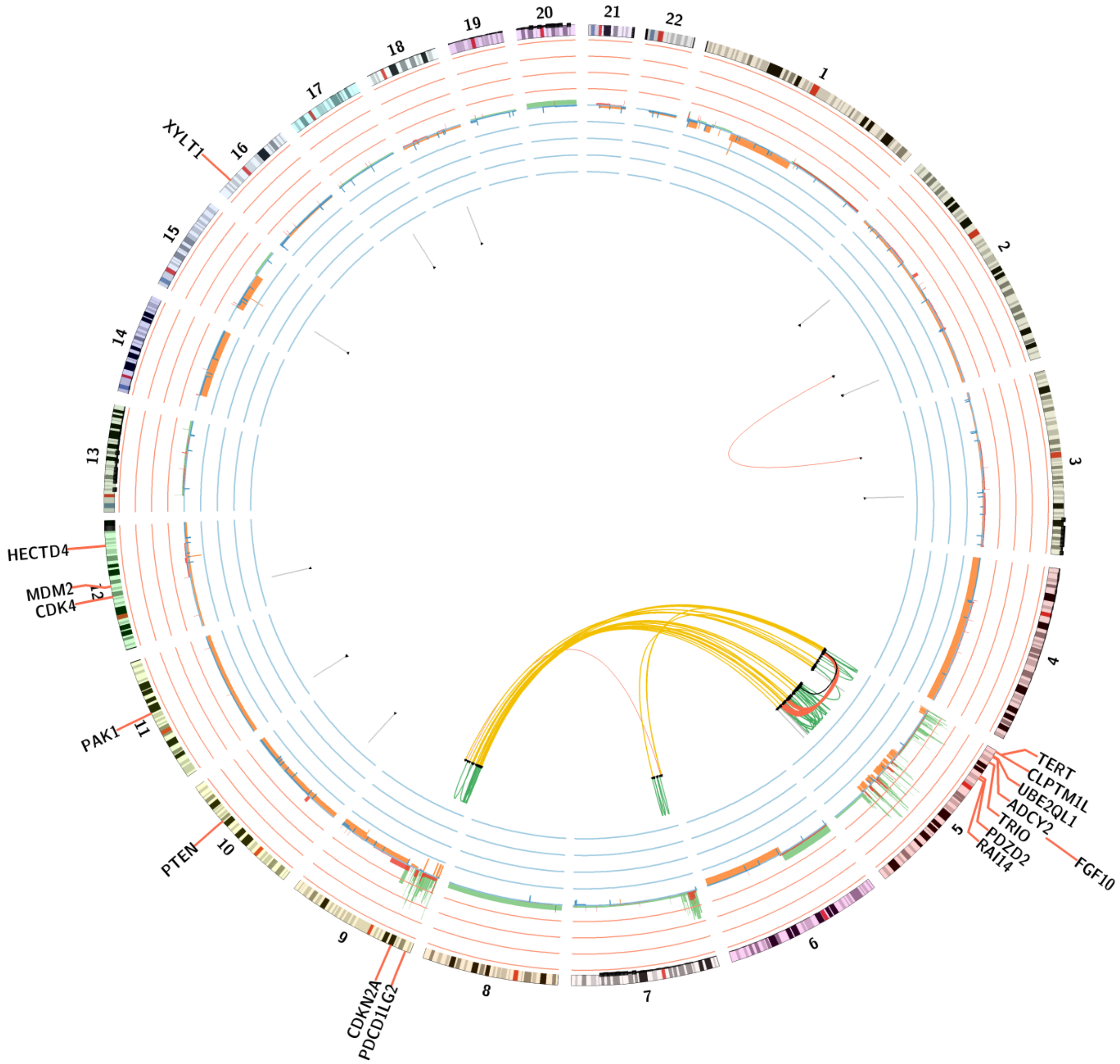
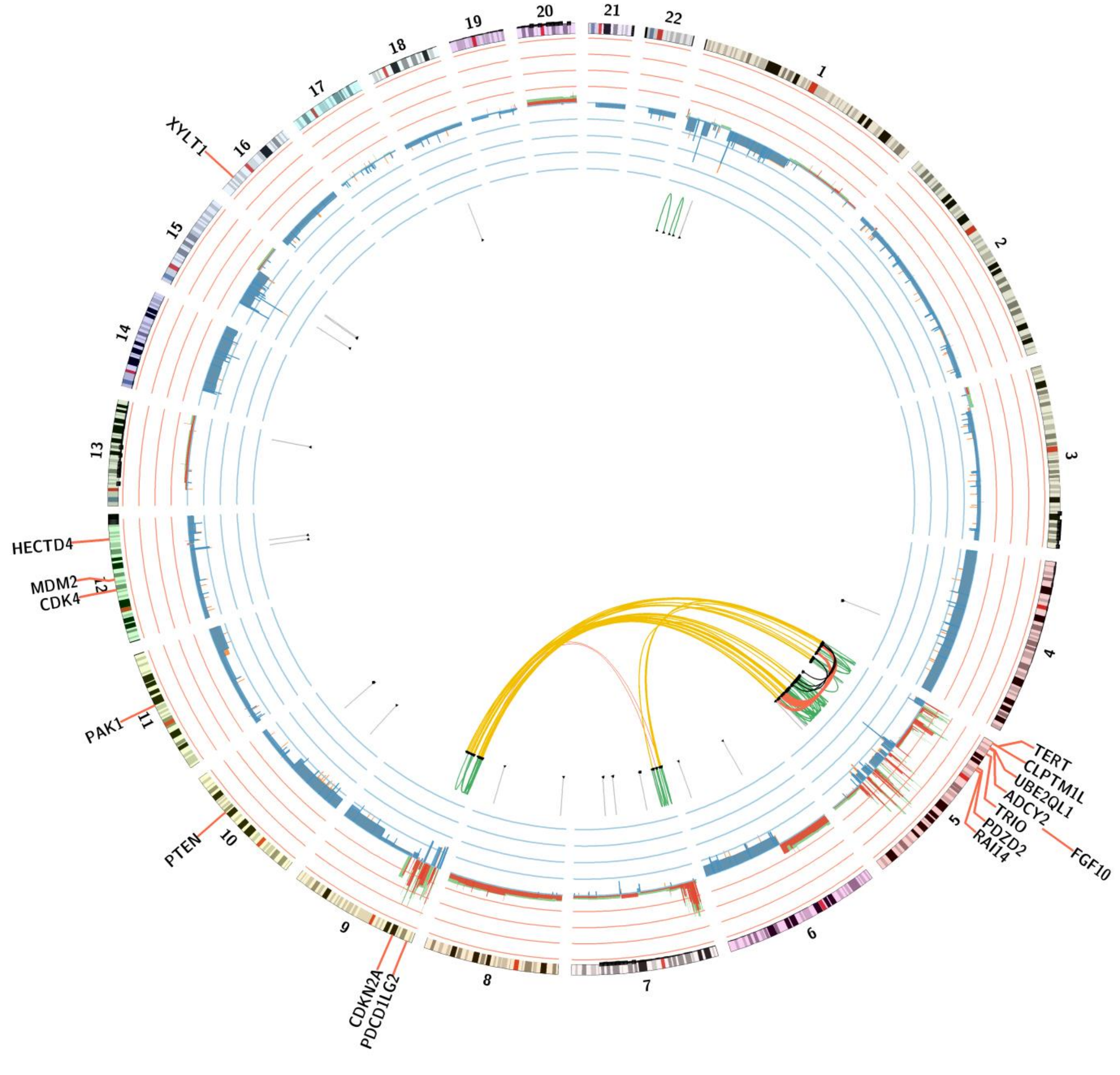
Patient 29 (sample 29a)



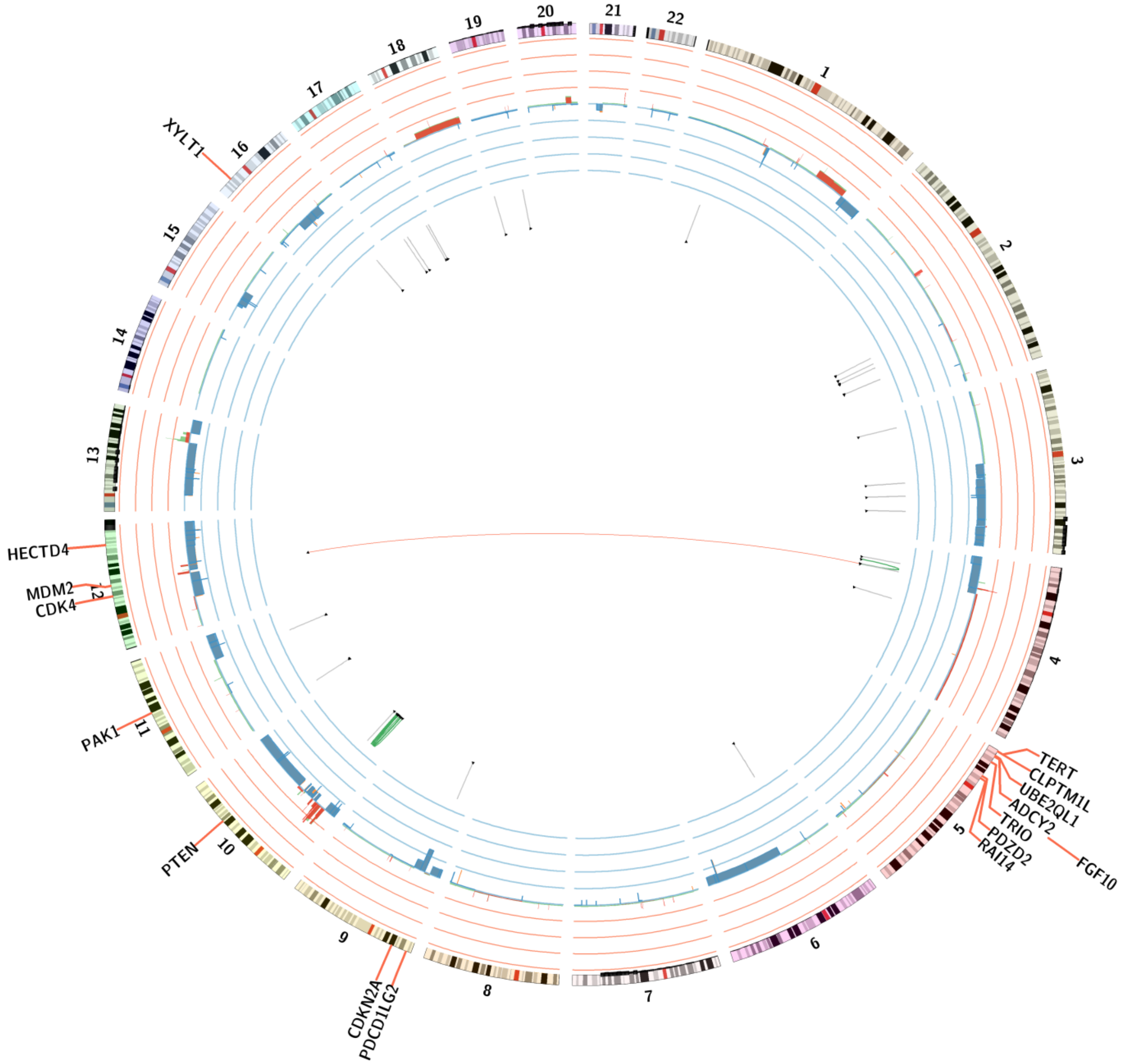
Patient 29 (sample 29b)



Patient 29 (sample 29c)



Patient 30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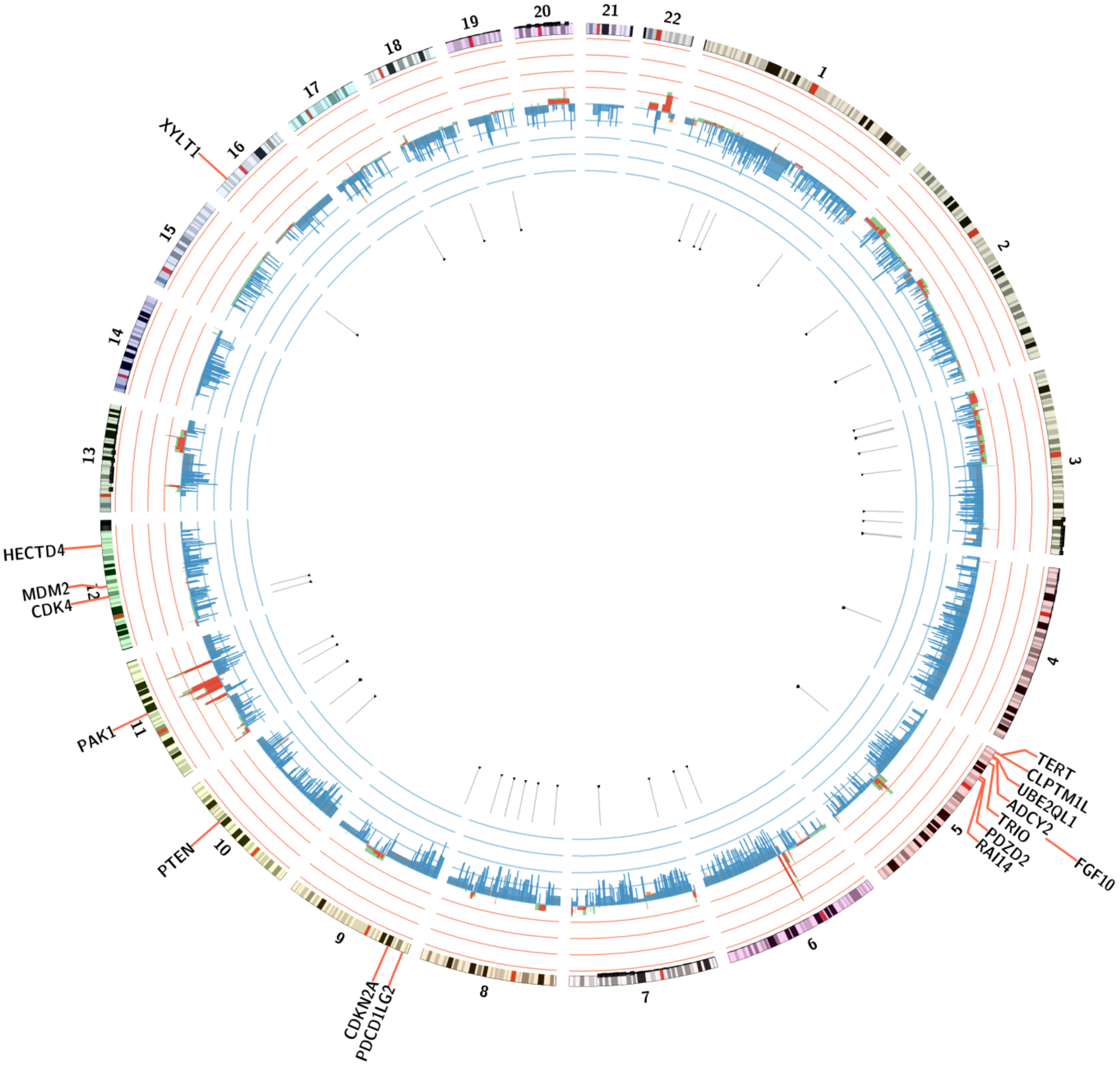
PDCD1LG2
PTEN
PAK1
MDM2
CDK4
HECTD4
XYLT1

Patient 31



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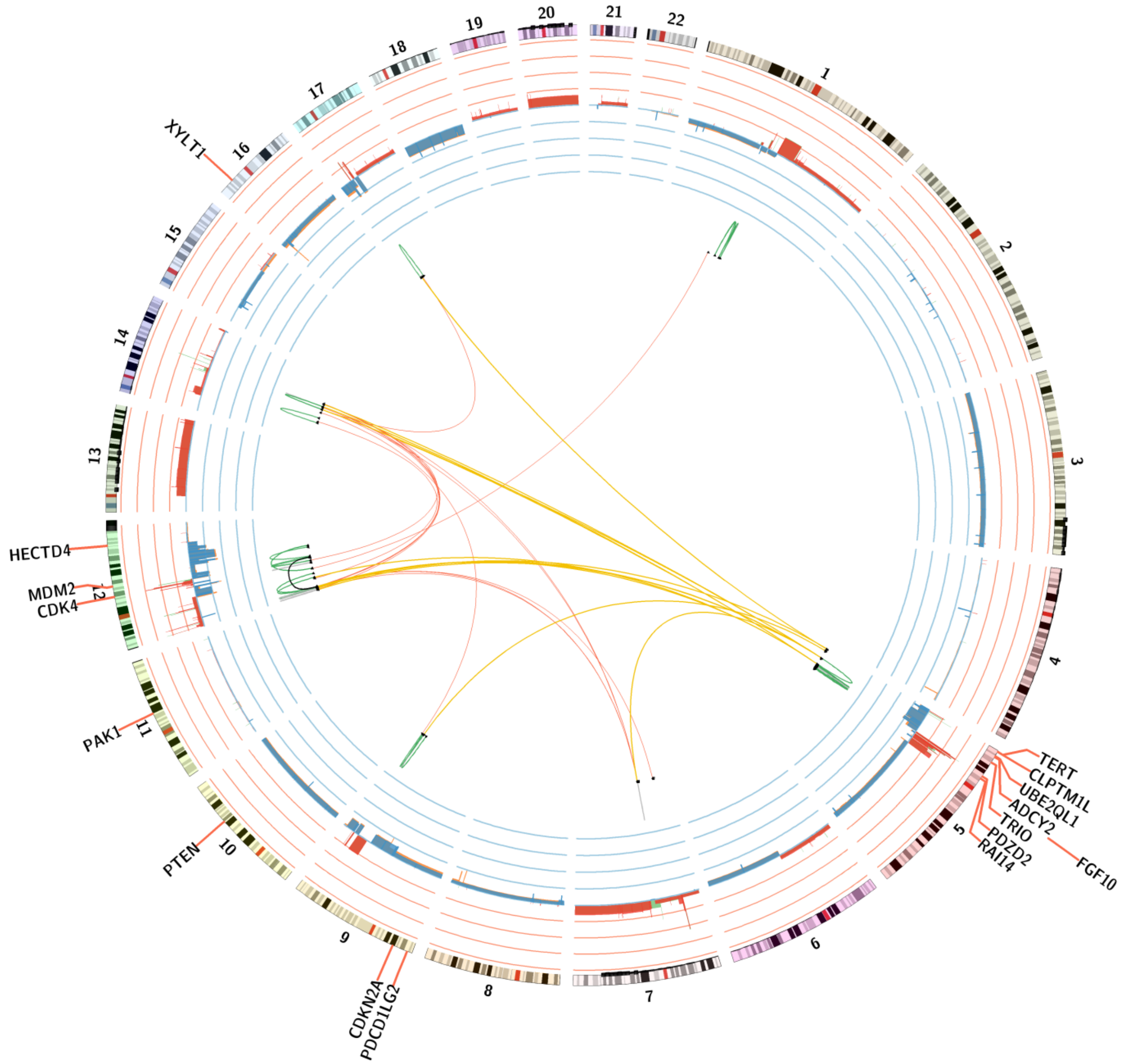
PDCD1LG2
PTEN
PAK1
MDM2
CDK4
HECTD4
XYLT1

Patient 32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CDK4
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HECTD4
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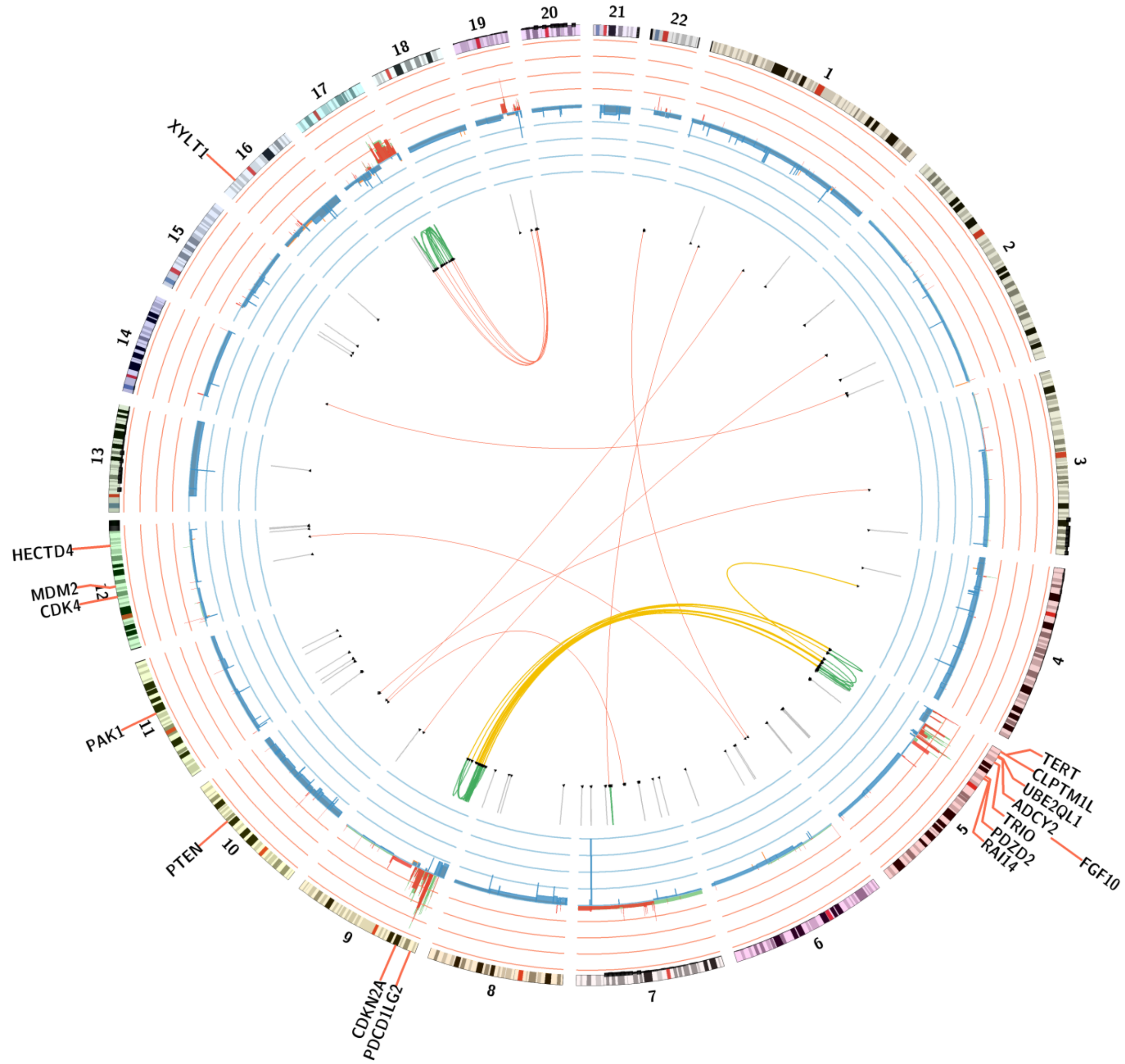
Patient 33



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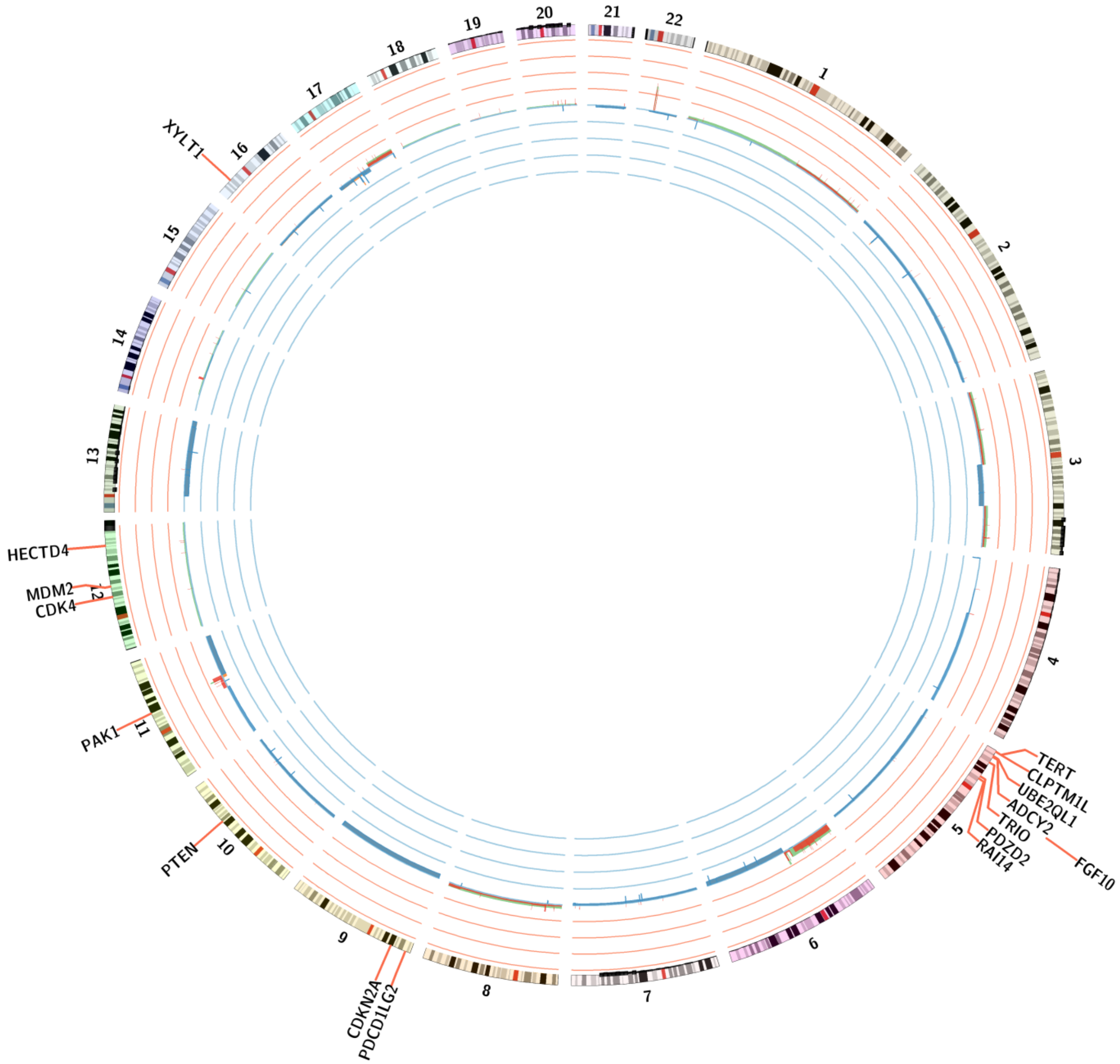
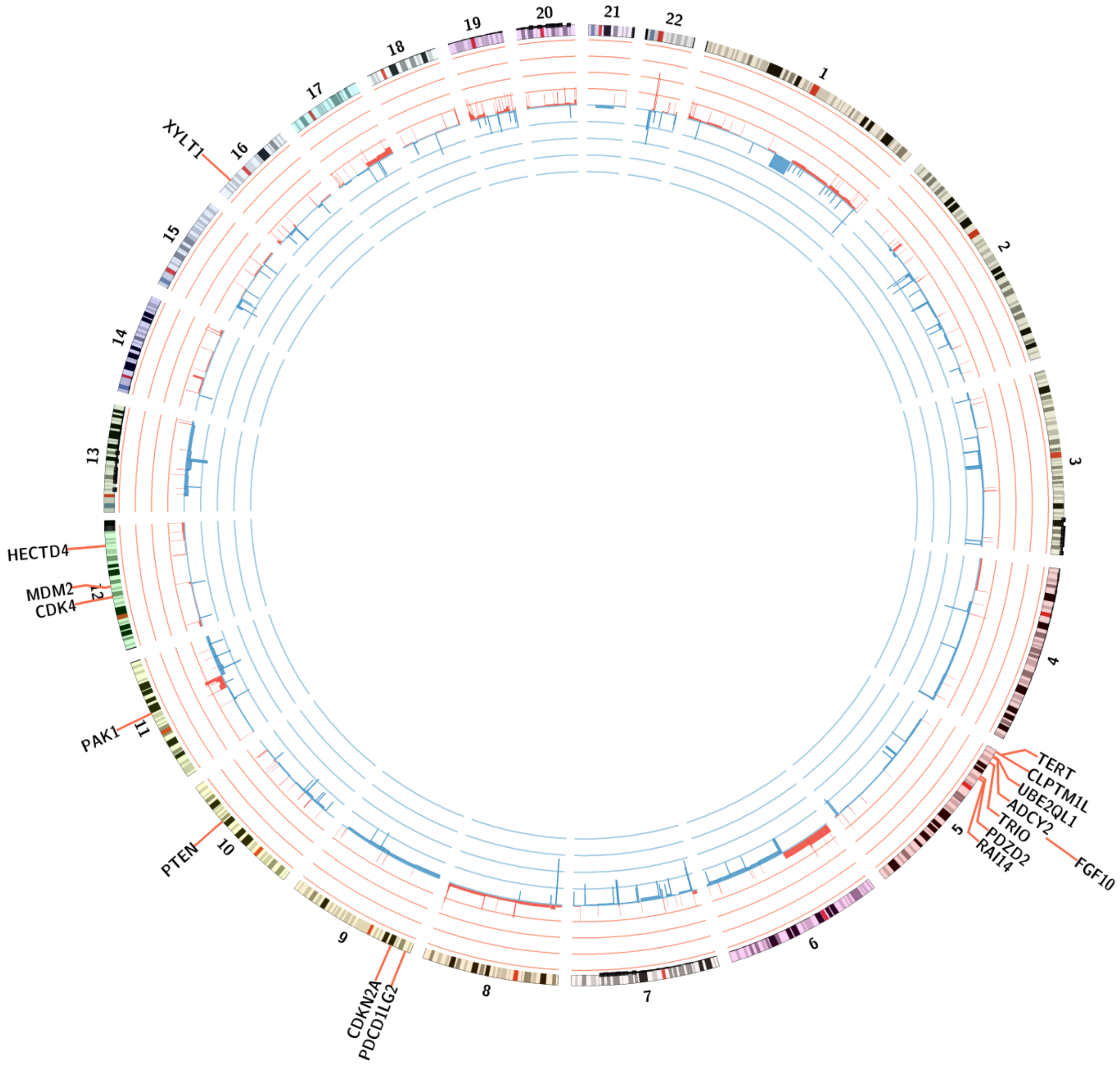
PAK1
CDK4
MDM2
HECTD4
XYLT1

Patient 34 (sample 34a)



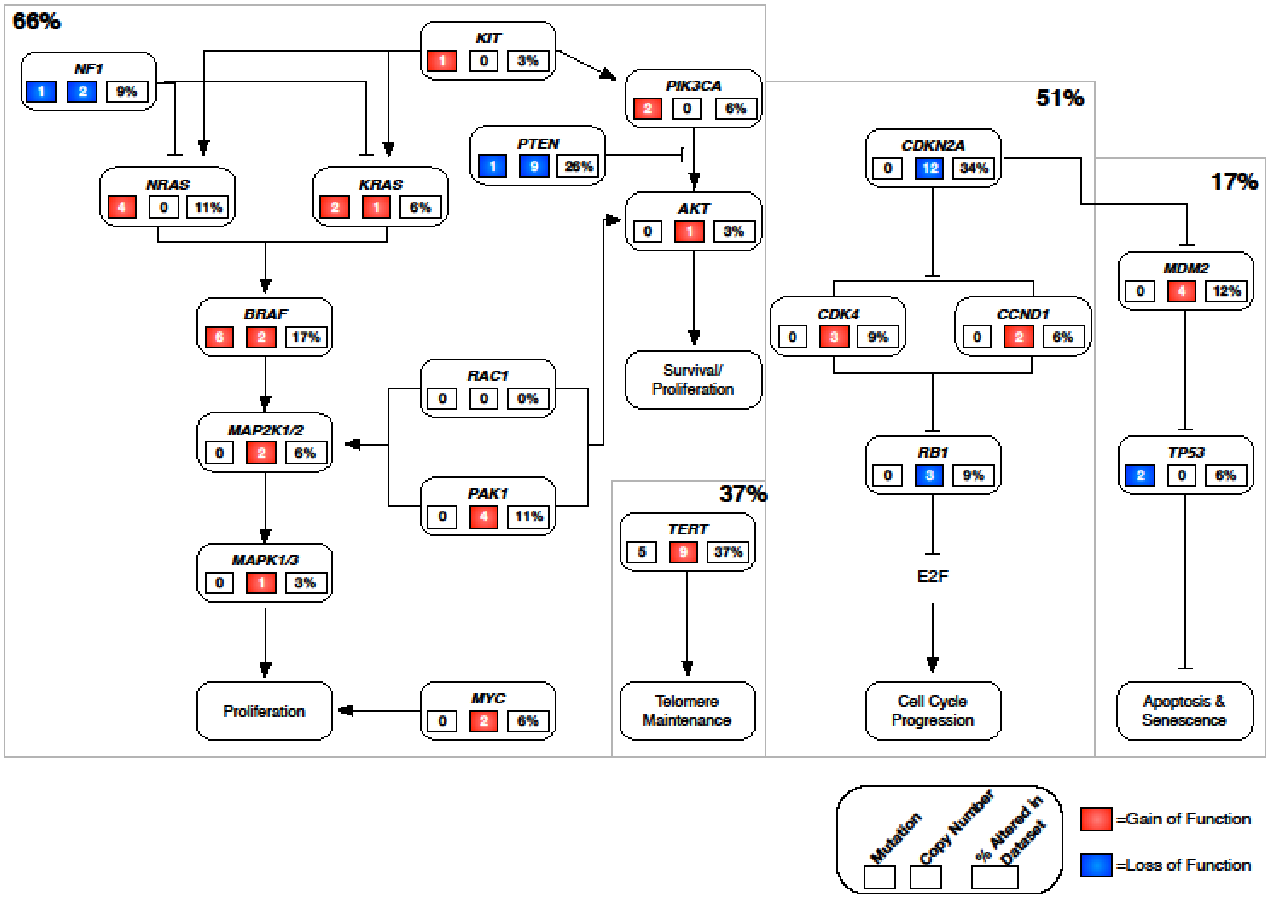
Patient 34 (sample 34b)



Supplemental Figure S4. Landscape of affected pathways in ALM

Supplemental Figure S4A. Impact of genomic events in ALM with respect to commonly altered melanoma pathways

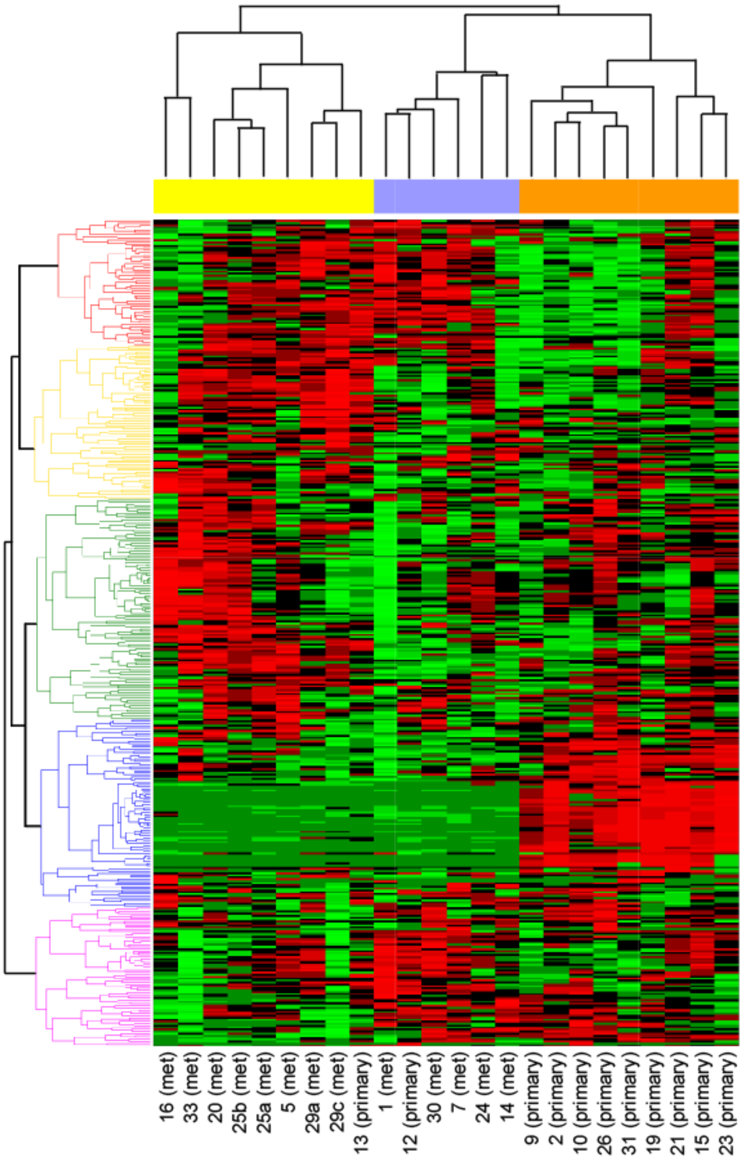
The percentage of patients impacted by respective pathways is shown in the upper corners of pathway boundaries. The numbers shown in gain/loss of function boxes indicate the number of patients impacted.



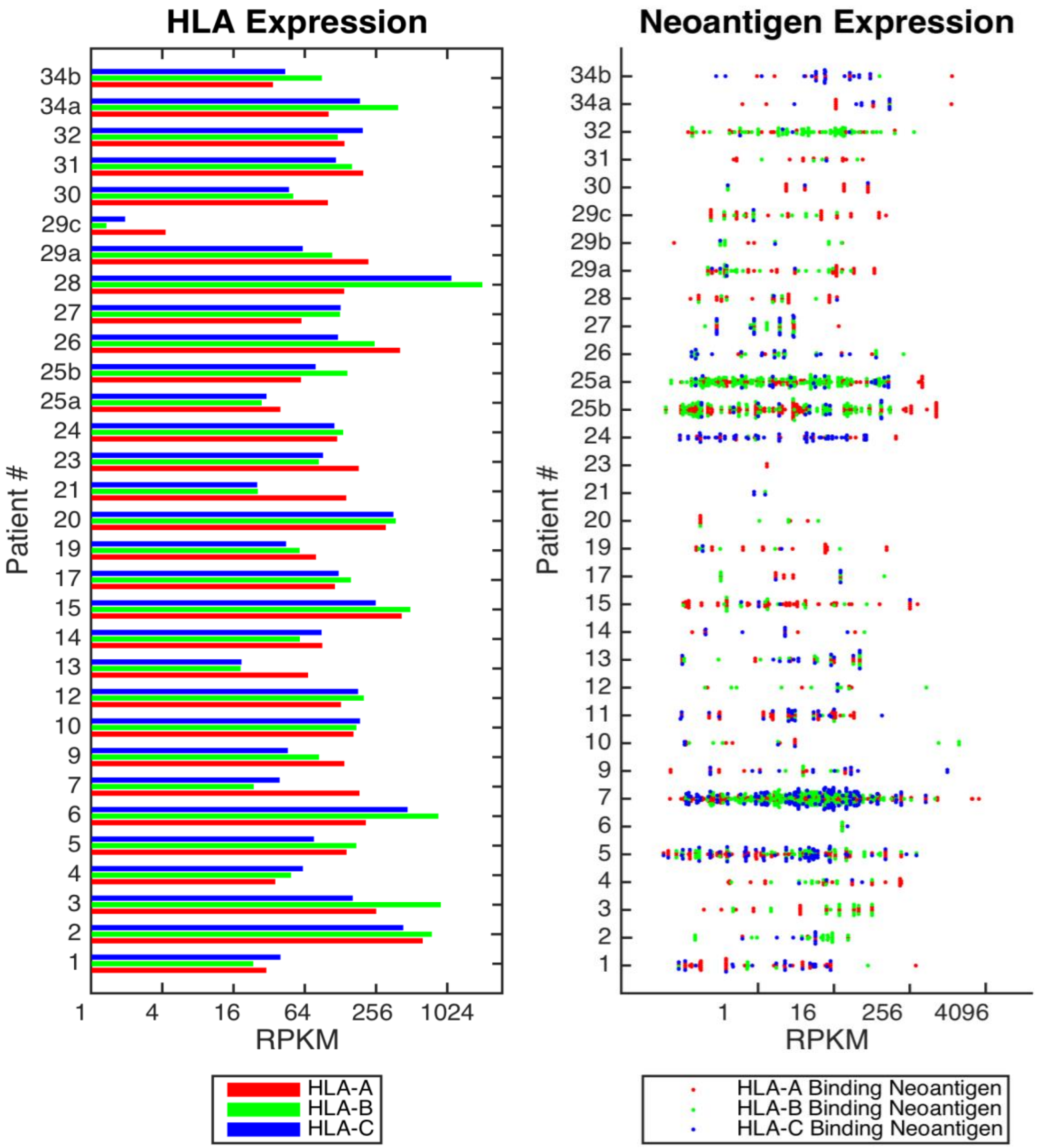
Supplemental Figure S4B. Unsupervised clustering of differentially expressed genes

Vertical dendrogram: Cluster_1 (red): Protein translation, ribosomal processes, NMD (nonsense mediated decay); Cluster_2 (yellow): ER stress response, NMD, RNA polymerase; Cluster_3 (green): Antigen presentation, Immune processes; Cluster_4 (blue): Chemotaxis, Keratinization, Intermediate Filament; Cluster_5 (pink): G2/M, pigmentation, NMD

Horizontal dendrogram: Clustering of ALMs visually revealed three subgroups as delineated by the yellow, purple, and orange color assignments. Patient IDs are shown at the bottom.



Supplemental Figure S5. Neo-antigen analysis of RNA-seq data



Supplemental Figure S6. Complex rearrangement on Chr 5p in patient 12

A CNV plot of chromosome 5 is shown, revealing a complex rearrangement occurring on the p arm and encompassing the *TERT* gene in patient 12's tumor. The y-axis represents the log2 fold of the tumor copy number over the normal.