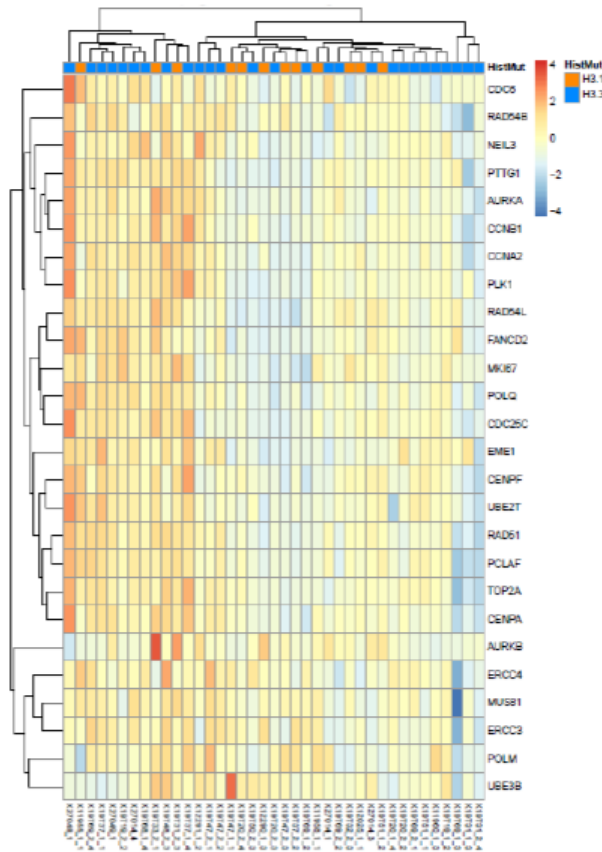


Supplementary Figure 1. Adult glioblastoma (aGBM) signatures. Lists and description of the genes composing the 52 DNA repair and cell-cycle gene expression signature identified in aGBMs as well as its refined 27-gene signature.

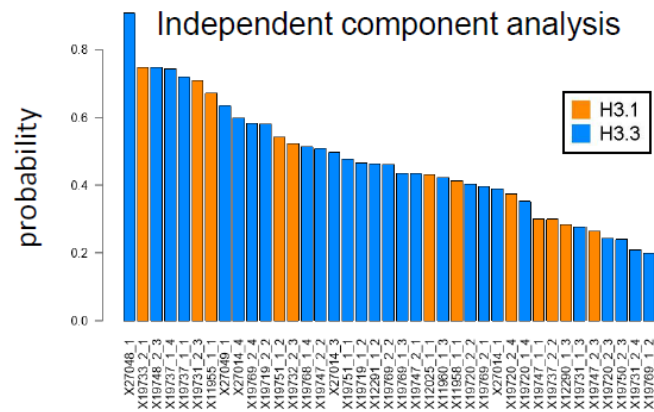
A <div> <u>AURKA</u> AURKB <u>CDC25C</u> CDC6 <u>CCNB1</u> CCNA2 <u>CDK1</u> CENPA CENPF <u>KIAA0101</u> MKI67 MAD2L2 PLK1 <u>PTTG1</u> <u>TOP2A</u> POLK POLM POLQ POLD1 REV1 RFC1 EME1 MUS81 BRCA2 HMMR MRE11A PALB2 RAD17 <u>RAD51</u> RAD54B RAD54L RAD50 RPA2 </div>	<div> DDB2 ERCC3 ERCC4 XPA XPC NEIL1 NEIL2 NEIL3 UBE3B <u>UBE2T</u> UBE3B <u>FANCD2</u> FANCF ATR MSH3 PMS1 RECQL5 SMUG1 NUDT1 </div>	B <div> <u>AURKA</u> AURKB <u>CDC25C</u> CDC6 <u>CCNB1</u> CCNA2 <u>CDK1</u> CENPA CENPF <u>KIAA0101</u> MKI67 PLK1 <u>PTTG1</u> <u>TOP2A</u> POLM POLQ EME1 MUS81 <u>RAD51</u> RAD54B RAD54L ERCC3 ERCC4 NEIL3 <u>UBE2T</u> UBE3B <u>FANCD2</u> </div>	<div> effectors and regulators of cell cycle cell cycle and DDR coordination of DDR DNA polymerases in NHEJ and DSB Holliday junction recombination HR single-stranded DNA break repair double-stranded DNA break repair NER NHEJ and NER Fanconi anemia MMR (MisMatch excision repair) BER </div>
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Supplementary Figure 2. (A). Heatmap of hierarchical clustering in the DIPG cohort based on the 27-gene aGBM signature. Illustrated is the lack of segregation of H3.1 and H3.3 tumors in separate groups based on the DNA damage repair and cell cycle gene expression signature. **(B-C)** ICA (Independent Component Analysis) of the cell cycle component in the DIPG cohort. Weight of the cell-cycle component from ICA of the DIPGs **(B)** showed no linkage with mutations in H3.1 K27M and H3.3. K27M specimens **(C)**.

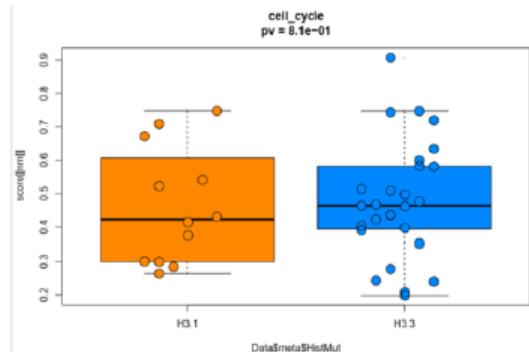
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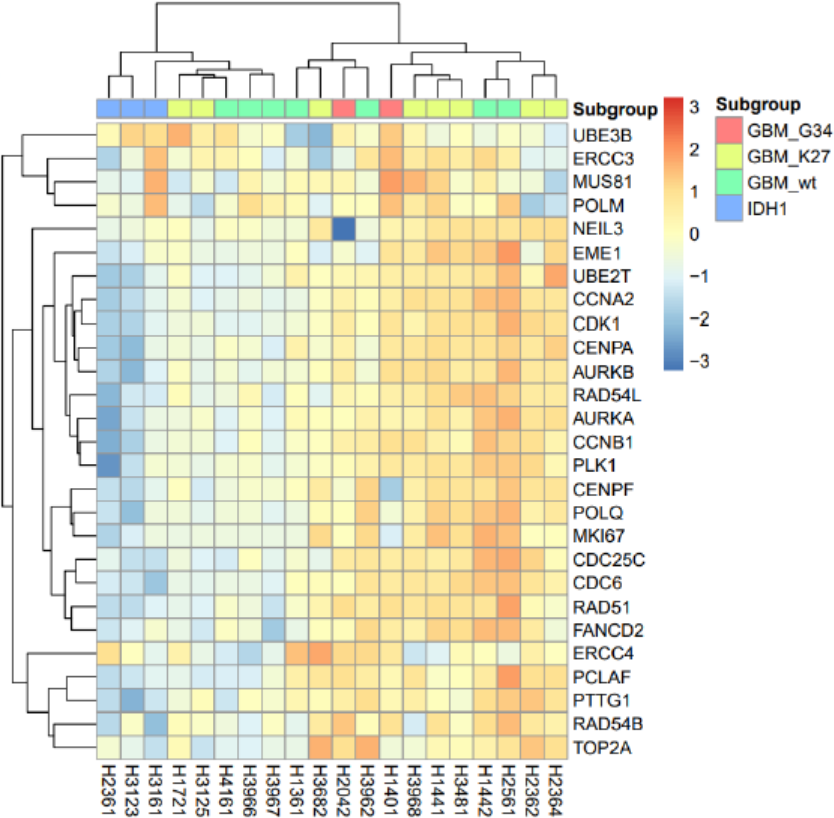
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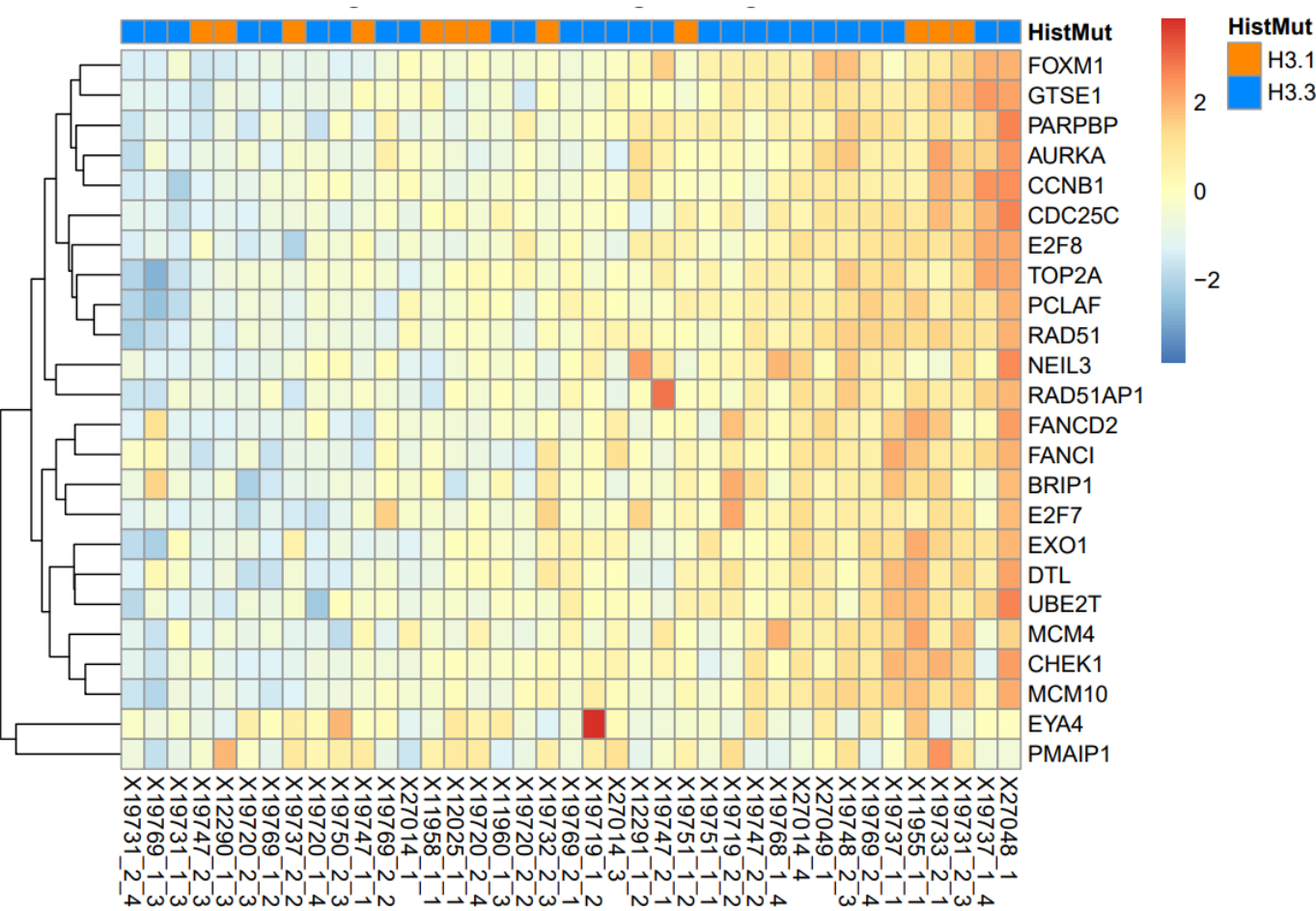
C



Supplementary Figure 3. Heatmap of hierarchical clustering in the sus-tentorial pHGG cohort based on the aGBM signature. Illustrated is the partial segregation of pHGG specimens into 2 groups based on the 27 DNA damage repair and cell cycle gene expression signature.



Supplementary Figure 4. Heatmap illustrating the partial segregation of DIPG specimens from a cohort containing H3.1 K27M and H3.3 K27M mutant samples based on the specific pHGG 28-DDR signature.



Supplementary Figure 5. Immunohistochemical analyses. Illustration of TMA HE slides and immunostainings on left side. Examples of PARP1, XRCC1, KI67, RAD51, MPG and APE positive immunostainings on right side (x40).

