Genome-wide Analyses Identify Recurrent Amplifications of Receptor Tyrosine Kinases and Cell Cycle Regulatory Genes in Diffuse Intrinsic Pontine Glioma

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Supplementary Figures

**Figure S1. The majority of LOH is associated with copy number losses**. A. Heat map showing copy number gains (red) and losses (blue), and copy neutral LOH (black) for (A) the whole genome, (B) chromosome 17p, from 36 DIPG compared with matched normal samples.

There are shared and distinct imbalances in paired samples from diagnostic and autopsy cases, indicated by asterisks. Diagnostic cases are designated "TD".

Figure S2: Focal gains of BRAF are found in 7/8 exophytic low-grade

brainstem gliomas, and none of 43 DIPGs. Heat map of segmented copy number data showing chromosome 7. Specific focal gains of a region on chromosome 7q34 extending from *KIAA 1549* to *BRAF was only seen in LGGs*. *The genes contained in the specific region of focal gain shown by the boxed region on the chromosome ideogram are shown at the bottom of the figure*. Copy number gains (red) and losses (blue) are shown in 43 DIPG (BSG) and 8 low-grade exophytic brainstem gliomas (LGG-BSG).

Figure S3: Focal gains of RTKs are associated with overexpression.

Maps of regions of gain and associated expression are shown for (A) PDGFRA, (B) MET and (C) IGF1R. The chromosome region containing focal amplifications, and the extent of amplification for each tumor is shown. The minimal common region of amplification is shown with a gray box, and genes within the minimal common region along with chromosomal position are shown below. Heatmap shows expression of all probes within the maximal region of amplification. The

minimal common region of amplification is shown with a gray bar in all panels. For the expression heatmap, expression of all genes within the maximum region of focal gain is shown for all tumors with available expression data. Genes contained in the common minimal region of gain are shaded in gray at the bottom of the heatmap. Tumors with focal gains identified by SNP analysis are labeled in red, tumors with scattered amplification identified only by FISH are labeled in purple, and tumors without evidence of copy number gain in this region are labeled in black. Overexpression of PDGFRA and IGF1R was seen in tumors with and without amplification. For PDGFRA, tumors with SNP-detected amplification showed 1.7-fold higher expression than tumors without amplification (p=0.1). For *IGF1R*, tumors with SNP-detected amplification showed 1.4-fold higher expression than tumors without amplification (p=0.2). MET overexpression was more specifically associated with amplification; tumors with SNP-detected amplification of *MET* showed 5.9-fold higher expression than tumors without amplification (p=0.001). (B) Tumor BSG001T contained a focal gain within a small region of *MET* that did not contain the probe sets used to detect *MET* expression. This very focal gain may indicate a genomic rearrangement of *MET* in this tumor.







TBXAS1

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Figure S3
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