**Supplementary Figure Legends**

**Figure S1.** A) Kaplan-Meier survival curve for *Ptch:p53+/+, Ptch;p53+/-,* and *Ptch;p53-/-* mice. B) Quantitation of GFD and GFI tumorsphere differentiation. Three random fields were counted (>500 cells per sample) from 3 independent lines of GFD and GFI tumorspheres differentiated in 1% FBS for 4 days. C) Injection of cultured GFD and GFI tumorsphere cells. 100,000 cells from 5 independent GFD and 6 independent GFI tumorsphere cells were injected into NSG mouse cerebella at passages indicated. D) Representative tumor histology of GFD and GFI tumorsphere injected tumors shown with H&E staining.

**Figure S2.** A) Kaplan-Meier survival curve comparing G2 mice injected 100 G1 tumor cells from NG, GFD, and GFI subtypes. B) Immunohistochemical analyses of G1 and G2 tumors with Ki67 (Novocastra NCL-L-Ki67-MMC: proliferation marker) and cleaved caspase 3 (Cell Signaling #9661: apoptosis marker) show no significant differences among the three subtypes. C) Serial self-renewal assays of 3 independent GFD and GFI tumorsphere lines each, showing long-term self-renewal potential.

**Figure S3**. Relative expression levels of the SHH pathway genes in G1 tumors of the three subtypes, measured by realtime RT-PCR. Each dot represents an independent tumor.

**Figure S4**: FISH analysis of G1 tumors that later evolved into GFI subtypes in vivo. Trisomy 6 cells are already abundant in these NG and GFD tumors, indicating that trisomy 6 precedes growth factor independent phenotype.

**Figure S5**. Top three pathways represented by the 465 genes analyzed in the Ingenuity pathway analysis tool. A) NG vs. GFI. B) GFD vs. NG.

**Figure S6.** H & E staining of G2 tumor injected with *Smo;GFAP-cre* tumor cells.