

## Supplementary Experimental Methods

**Transfections and plasmids.** For transfections, plasmids used were pEF-EGFP (the kind gift of R. Kageyama, Kyoto; Paquin et al., 2005), pEF-GM (empty vector; from R. Kageyama), and pSUPER-scrambled shRNA as a control. For the SHP-2 constructs, C-terminal HA-tagged forms of human wildtype (WT)-SHP-2, D61G-SHP-2 or dominant-negative ( $\Delta$ P-SHP-2) (Tang et al., 1995) were subcloned into the pEF-GM vector. The shRNAs were cloned in the pSuperiorRetroPuro vector (OligoEngine), and the sequences were:

1 -

5'ATCCCCGATTCAGAACACTGGGGACTTCAAGAGAGTCCCCAGTGTTCTGAA  
TCTTTTTGGAAA3'

2 -

5'GATCCCCGAGTAACCCTGGAGACTTCTTCAAGAGAGAAGTCTCCAGGGTTA  
CTCTTTTTGGAAA3'.

For transfections, within two hours of plating, precursors were transfected using Fugene6 (Roche), mixing 0.33  $\mu$ g pEGFP and 0.66  $\mu$ g of pEF-GM, pSUPER-scrambled shRNA, pSUPER-SHP-2 shRNA1 or shRNA 2, or 1 $\mu$ g of pEF-DPSHP-2, pEF-WTSHP-2 or pEF-D61GSHP-2, , 1.5  $\mu$ l Fugene6 and 100 $\mu$ l OptiMEM (Invitrogen). NIH 3T3 cells were transfected at 80% confluency with Lipofectamine 2000 (Invitrogen).

**Antibodies.** Primary antibodies used for immunolabeling were mouse anti-GFP (1:1000, Molecular Probes), rabbit anti-GFP (1:400, Chemicon), chicken anti-GFP (1:1000, Molecular Probes), mouse and rabbit anti-HA (1:400, Covance), rabbit anti-SHP-2 (1:500, Santa Cruz Biotechnology), mouse anti-nestin (1:400, Chemicon), mouse and rabbit anti- $\beta$ III tubulin/Tuj1 (1:1000, Covance), rabbit anti-GFAP (1:800, Chemicon), mouse anti-HuD (1:200, Molecular Probes), rat anti-CD44 (1:200, Chemicon for tissue sections or 1:400, BD-Pharmingen for cultured cells), rabbit anti-phosphoSTAT3-Tyr705 (1:200 Cell Signaling Technology), rabbit anti-phosphoERK-Thr185/Tyr187 (1:500, Cell Signaling Technology; 1:500, Promega), mouse anti-Ki67 (1:200, BD Bioscience). Secondary antibodies used for immunocytochemistry were indocarbocyanine (CY3)-

conjugated goat anti-mouse or anti-rabbit IgG (1:400), FITC-conjugated anti-mouse or anti-rabbit IgG (1:100, Jackson Immuno Research Laboratories), Alexa Fluor 555 goat anti-rat (1:1000, Molecular Probes), Alex Fluor 350 goat anti-mouse (1:500, Molecular Probes), DTAF-conjugated streptavidin (1:2000), and CY3-conjugated streptavidin (1:2000, Jackson ImmunoResearch Laboratories). Primary antibodies used for biochemistry were rabbit anti-SHP-2 (1:500, Santa Cruz Biotechnology), and anti-ERK (1:5000, Santa Cruz Biotechnology). The secondary antibody used for biochemistry was HRP-conjugated goat anti-rabbit (1:5000, Biorad).