SUPPLEMENTARY METHODS

Reverse transcription and quantitative PCR. Total RNA was isolated using an RNeasy Mini Kit (Qiagen). The first strand cDNAs was generated using SuperScript™ III First Strand RT-PCR kit (Invitrogen). The cDNAs were PCR amplified with human Notch receptors and ligands specific primers. The primer sequences are given as follows:

Notch1 (5' GCA GAC TAT GCC TGC AGC TG 3' and 5' GCC ACA CTC GTT GAC ATC CTG 3')
Notch2 (5' CAG TGT GCC ACA GGT TTC ACT G 3' and 5' GCA TAT ACA GCG GAA ACC ATT CAC 3')
Notch 3 (5' CGC CTG AGA ATG ATC ACT GCT TC 3' and 5' TCA CCC TTG GCC ATG TTC TTC 3')
Notch 4 (5' ATG ACC TGC TCA ACG GCT TC 3' and 5' GAA GAT CAA GGC AGC TGG CTC 3')
Dll1 (5' CTA CAC GGG CAG GAA CTG CAG 3' and 5' CGC CTT CTT GTT GGT GTT CTT G 3')
Dll3 (5' CTC TTC TTC AGA GTC TGC CTG AAG 3' and 5' TCC TAA CTC CTC TCT CCA GGT TTC3')
Dll4 (5' CGG GTC ATC TGC AGT GAC AAC 3' and 5' AGT TGA GAT CTT GGT CAC AAA ACA G 3')
Jag 1 (5' GCT TGG ATC TGT TGC TTG GTG AC 3' and 5' ACT TTC CAA GTC TCT GTT GTC CTG 3')
Jag2 (5' GCT ATT TCG AGC TGC AGC TGA G 3' and 5' GCG GCA GGT AGA AGG AGT TG 3')

Quantitative PCR was also performed using the Taqman system (Applied Biosystems) following the manufacturer's specifications, using primers designed not to amplify genomic DNA. When mRNA levels from tumors were analyzed, GeNorm (MedGen) was used to select the normalization values out of 6 housekeeping genes: Beta-Actin Hs99999909_m1, HMBS Hs00609297_m1, UBC Hs00824723_m1, Cyclin D Hs00277039_m1, and 18S Hs99999901_m1, GAPDH Hs99999905_m1 Applied Biosystems). For *in vitro* analysis, Beta-Actin Hs99999909_m1 (Applied Biosystems) was used as a loading control. Other primers used: Notch1 Hs01062014_m1, Hes1 Hs00172878_m1, Hey1 Hs00232617_m1 (Applied Biosystems). All assays were run in a 7300 Applied Biosystems Real-Time PCR using 7300 SDS v1.3.1 (Applied Biosystems).

BrdU Proliferation Assay. Tumor cell proliferation was measured using BrdU cell proliferation kit (Millipore). Briefly, 1×10^4 cells were seeded per well of a 96 well plate in growth media and incubated with BrdU reagent (Millipore) for 24 h. Amount of BrdU labeling, was determined immunochemically using anti-BrdU antibody followed by addition of goat anti-mouse IgG-peroxidase conjugated secondary antibody, substrate and stop solution. The OD was measured at 450 nm.

***In vivo* BrdU assay.** BrdU-PBS (10mg/ml) was injected intraperitoneally in Notch1$^{+/-}$ or Notch1$^{+/+}$ mice, sacrificed after 24hr and liver tissues fixed in 4% paraformaldehyde, and immunostained with an anti-BrdU antibody (Abcam).

Migration and Invasion Assays. Tumor cells were seeded at 3×10^4 cells/well to the insert of the upper chamber of CytoSelect™ 24-Well Cell Migration Assay plate (8 μm pore size, Cell Biolabs, INC) in RPMI 1640 without serum. The same media with 10% FBS was then added to the lower chamber. After incubation period of 24 h, cells from the inside of the upper chamber were removed by swabbing with a wet cotton stick. The inserts were then stained in Cell stain solution. The membrane was removed from the insert and mounted on slides for imaging and quantification. The number of migrating cells was determined by counting cells in 8 random fields from 3 inserts through 40X magnification. Invasion assay was performed similarly using BD BioCoat™ Growth Factor Reduced BD Matrigel™ Invasion Chamber, 8.0 μm PET (BD Bioscience)

Adenovirus production and Injection. The adeno-Fc or Adeno-N1ECDFc (pAdlox-Notch1$^{1-36}$) was grown in HEK293 cells, as previously described {Hardy, 1997 #49}. Briefly, HEK293 cells were harvested 48 hrs after infection, lysed by freeze-thawing, and isolated in a CsCl gradient. The virus was then dialyzed 3 times, then titrated by serial dilutions incubated on 293T cells, followed by staining using NCL Adeno (Novocastra, UK) goat-anti-mouse, FITC conjugated

(Sigma). 1X10^9 viral particles per mouse were injected retro-orbitally, 4 days prior to intracardiac injection of NGP cells. For the investigation of in vivo tumor cell arrest or attachment to liver, 10^5 NGP-luc cells were injected intracardially into nude mice expressing Fc or N1D. Mice were sacrificed after 24 hr and the livers were subjected to *ex vivo* bioluminescence imaging.

siRNA transfection. NGP cells were transfected with 50nM ON-Target*plus* Jagged1 siRNA or negative control ON-TARGET*plus* Non-targeting Control Pool siRNA (ThermoScientific) using DharmaFECT1 transfection reagent.