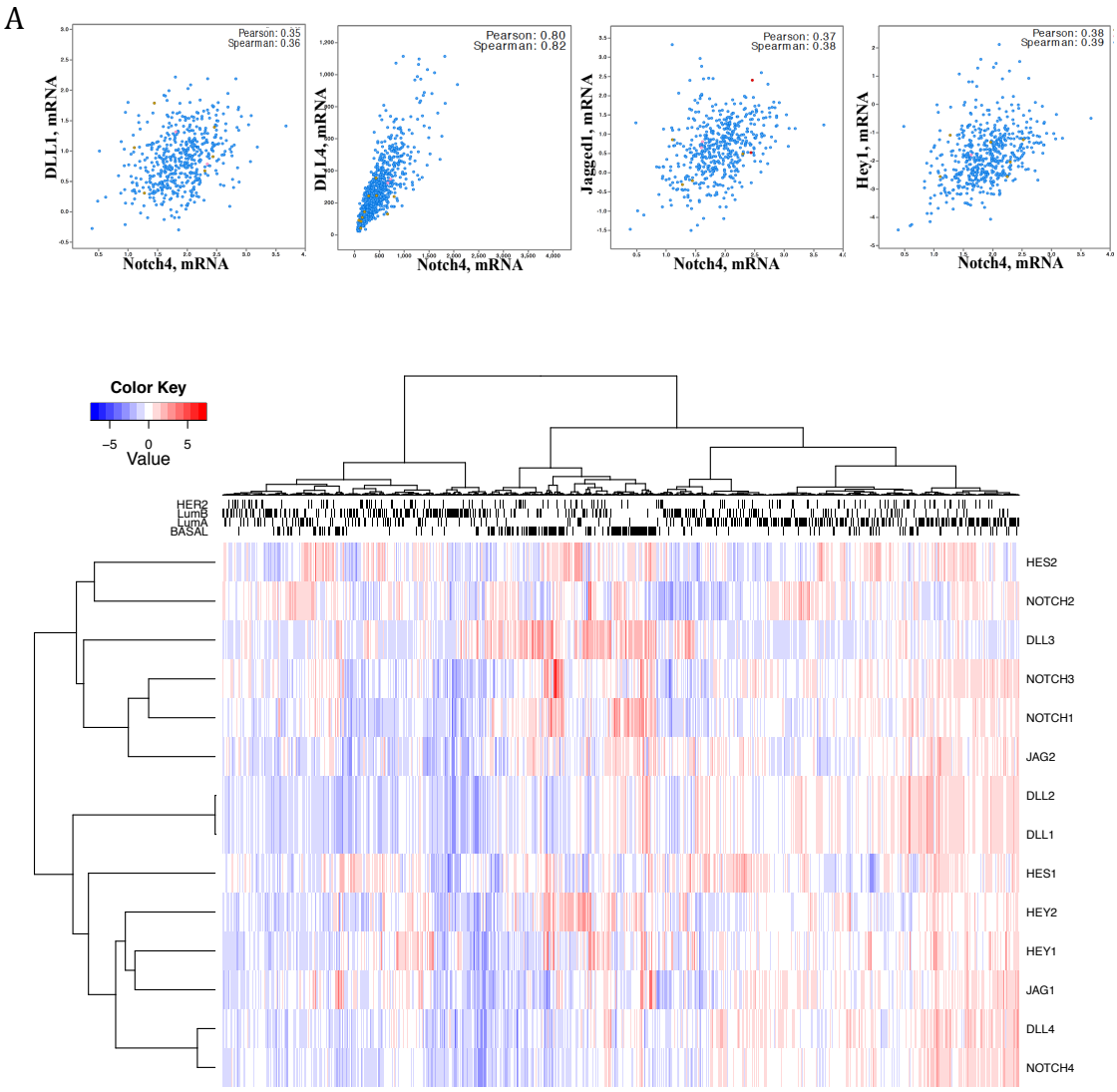
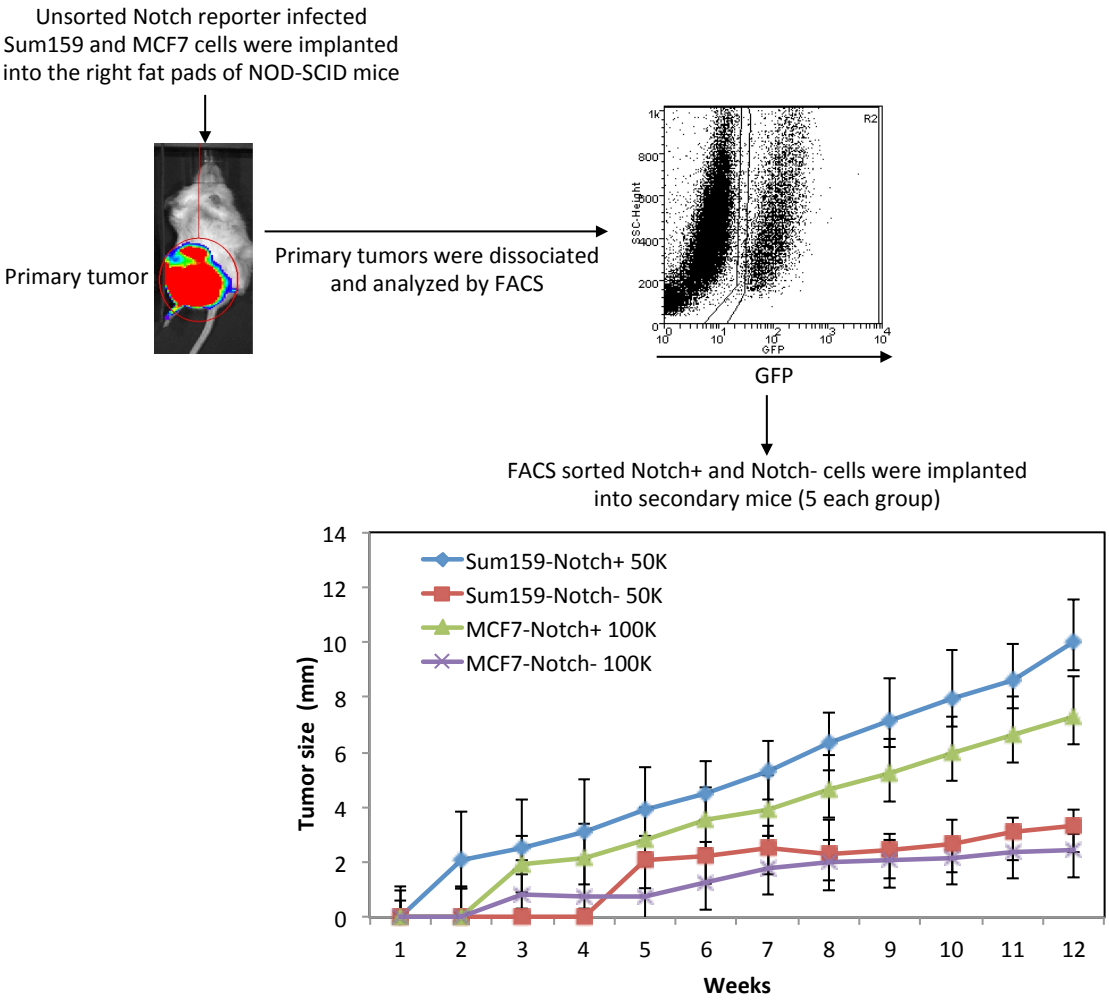
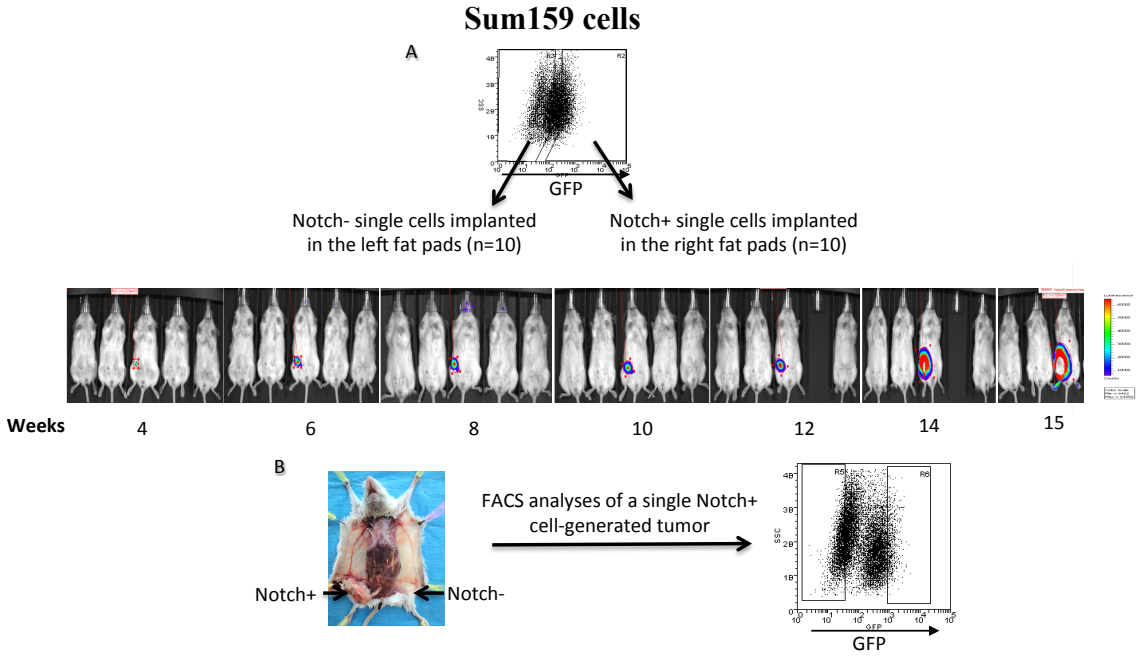
Supplemental Data



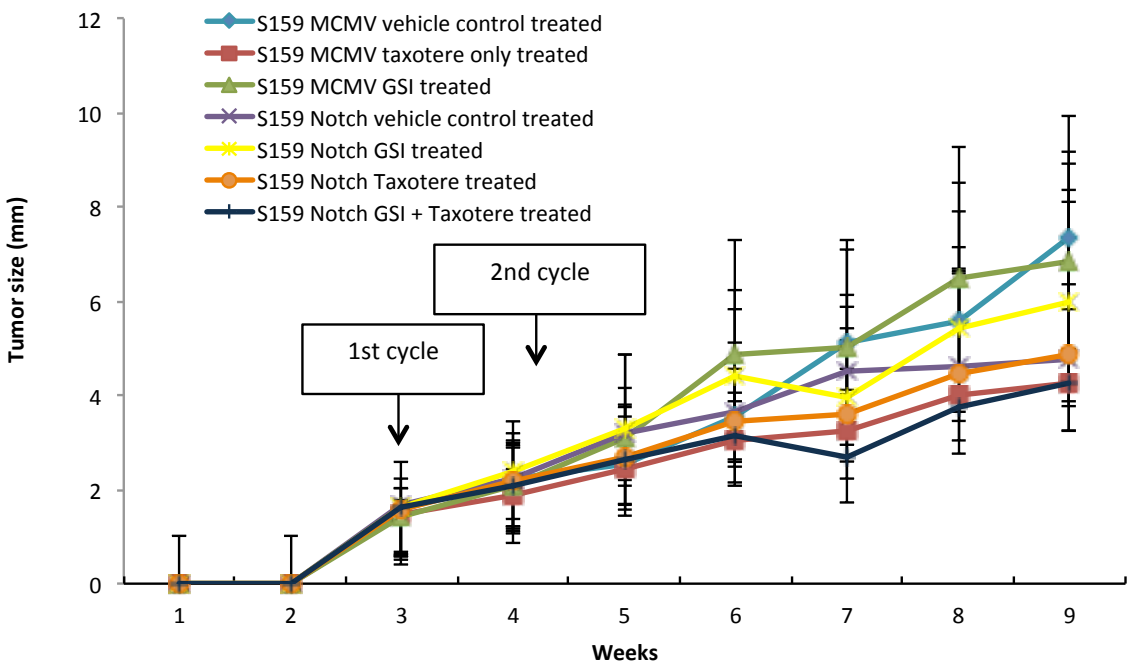
Supplemental Figure 1. Notch4 mRNA expression correlates with Notch ligands and downstream effectors. A) TCGA analyses of breast cancer data set utilizing the cBioPortal show a positive correlation between the Notch4 mRNA expression and DLL1, DLL4, Jagged1 and Hey1 mRNA expressions. **B)** Heat map analyses showing that Notch4 with Hey1, Hes1, Hey2, DLL1, DLL2, DLL4, JAG1



Supplemental Figure 2. A schematic outline of experimental procedures. Unsorted Sum159 or MCF7 cells expressing Notch reporter implanted into the fat pads of NOD-SCID mice and the resulting tumors were dissociated and analyzed by flow for GFP expression. GFP+ (Notch active) and GFP- (Notch inactive) cells were Flow sorted and re-implanted into the animals and the tumor growth is monitored.



Supplemental Figure 3. A single Notch+ cell has the capacity to generate tumors that represents the initial heterogeneity. (A) FACS sorted single Sum159 Notch+ (n=10) or Notch- (n=10) cells were implanted into the fat pads of NOD-SCID mice. Notch activity and tumor growth were monitored by bioluminescent imaging in live animals. One out of ten implantation of Notch+ single cells was able to grow tumor and showed a strong Notch activity *in vivo*. **(B)** When single Notch+ cell generated tumor was FACS analyzed, it showed a similar phenotypic heterogeneity of primary tumors.



Supplemental Figure 4. Evaluation of tumor growth following the treatment of animals with GSI, Docetaxel or combination treatments. Sum159 cells expressing Notch reporter implanted into the fat pads of NOD-SCID animals and the first cycle of treatment was started at 3 weeks post implantation and repeated after one week. Animals were terminated after 9 weeks for analyses.