**Supplementary Figure 1:**

**A,** Confirmation of estrous synchrony of experimental mice via vaginal lavage followed by staining with 0.1% crystal violet. **B,** Schematic depicting location of tumor-adjacent tissue with contralateral control tissue. Images were taken of intraductal injections of ZsGreen-labeled PNA.Met1 cells. White dashed line labeled ‘DCIS-like’ indicates tumor growth resembling DCIS. White dashed line labeled ‘IDC’ indicates tumor growth resembling invasive ductal carcinoma. **C,** Trypan blue-labeled ZsGreen PNA.Met1 tumor cells in the mammary ducts at time of collection (brightfield and fluorescent, top left and top right, respectively) with histology of intraductal injection model shown below. **D,** Schematic depicting FACS gating strategy.

**Supplementary Figure 2:**

**A,** MA-plot of count data from Zhang\_RNAseq analyzed using the DESeq2 package showing 17,877 DEGs, each represented by a dot. Red dots indicate adjusted p-value < 0.1. **B,** Principle component analysis (PCA) completed on the top 1000 DEGs (ranked by adjusted p-value). Red circles represent control (n = 3); blue circles represent TAG (n = 3). **C,** Key enrichment plots from GSEA listed for control glands (top) and TAG (bottom).

**Supplementary Figure 3:**

**A,** Right, Western blot analysis of STAT1 in CAF cells treated with siRNA targeting STAT1 (siSTAT1, right lane) or non-silencing control (control, left lane). Left, Western blot analysis of STAT1 in CAF cells transfected with one of two STAT1-targeting shRNA constructs (23.1 and 26.1) or control (left lane). **B,** Quantifications from EdU proliferation assay of CAFs treated with siSTAT1 or non-silencing control siRNA. **C,** Principle component analysis (PCA) of 68 cytokines showed a 39% total variance of the first component (PC1) and 22% total variance of the second component (PC2). **D,** Heat map of top differential secreted factors in siNS CAF conditioned media (CM) compared to siSTAT1 CAF conditioned media. **E,** Western blot analysis of PTX3 expression in PTX3-depleted CAF cells (siPTX3) compared to CAF cells transfected with a non-silencing control siRNA (siNS).

**Supplementary Figure 4:**

**A,** IHC showing vehicle-treated tumors display higher expression of STAT1 that drug-treated tumors. Single-treated doxorubicin tumors display higher STAT1 expression compared to single-treated fludarabine tumors and combined-treated tumors. **B,** Quantification of STAT1+ cells per 40X field of view.

**Supplementary Figure 5:**

Proposed Model of a Vicious Cycle of Tumorigenesis facilitated through stromal STAT1. 1) Tumor initiation stimulates CAF and stromal stem cell. 2) Increased expression of stromal STAT1 in CAF promotes tumorigenesis by activating secretion of PTX3. 3) PTX3 promotes CAF proliferation via autocrine signaling. 4) Expanded CAF promotes further tumor proliferation.