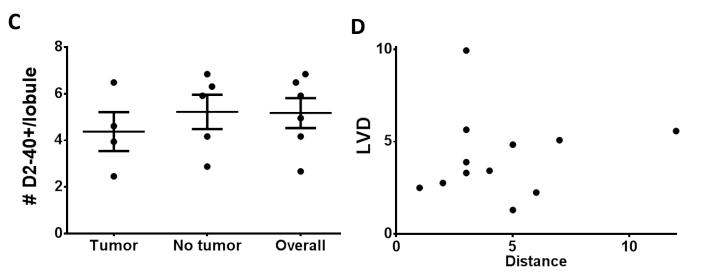
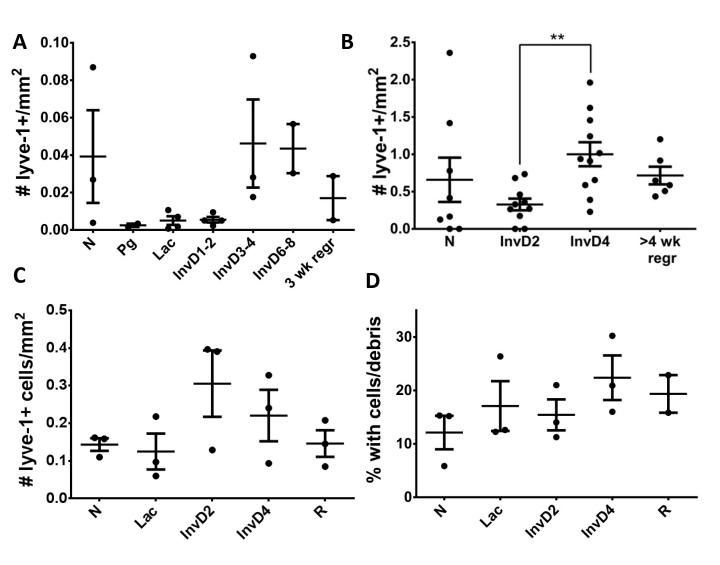


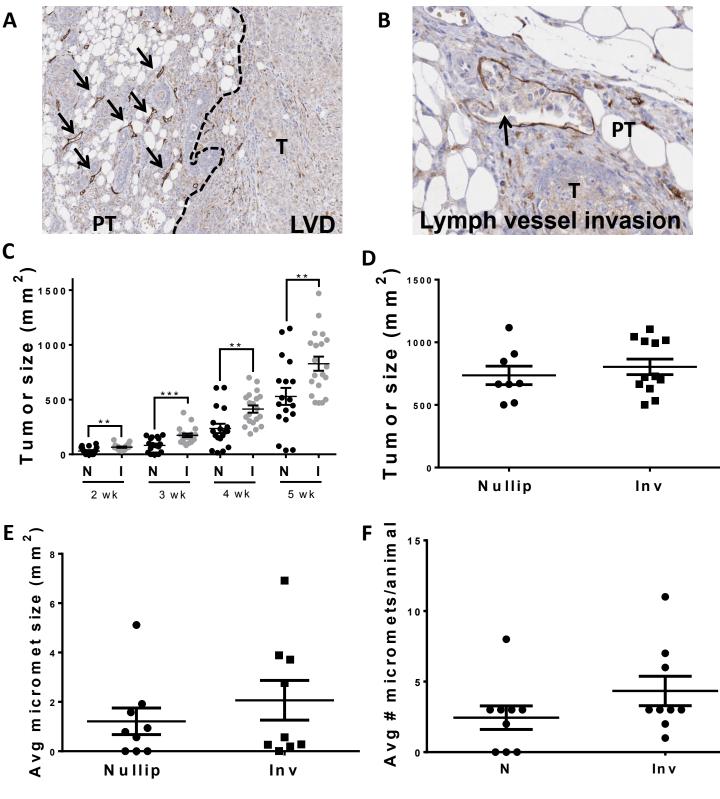
Number of Cases Each Category (% each category)						
Group	LumA	LumB	Her2	TN	Total (n)	Avg LVD
NBP	4 (40%)	2 (20%)	1 (10%)	3 (30%)	10	3.15271
≤3	4 (40%)	2 (20%)	1 (10%)	3 (30%)	10	5.910766
>3≤6	4 (44%)	2 (22%)	1 (11%)	2 (22.2%)	9	4.257532
>6≤10	4 (40%)	2 (20%)	1 (10%)	3 (30%)	10	3.901056
>10≤15	4 (44%)	2 (22%)	1 (11%)	2 (22.2%)	9	3.402957
>15	4 (50%)	2 (25%)	1 (12.5%)	1 (12.5)	8	2.521483



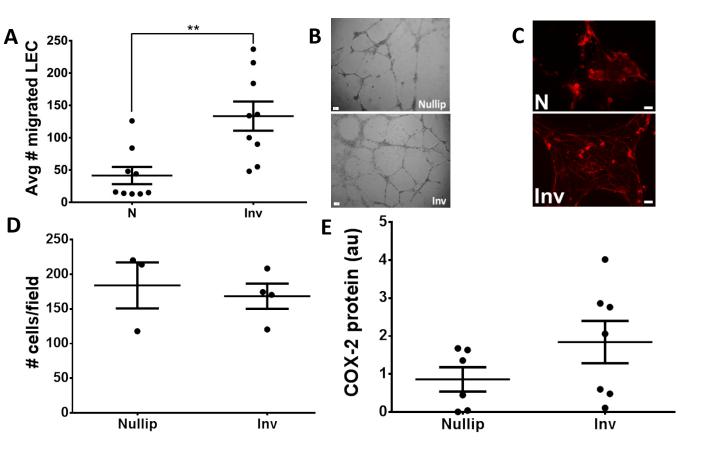
Supplemental Figure 1: A) Tumor size in the nulliparous (nullip) and <2 years postpartum (PP)groups. **B)** Reproductive category and biologic subtype of the clinical cohort used to analyze lymphatic vessel density and lymphatic invasion in postpartum cases. **C)** Analysis of LVD in normal tissues from women <1 year postpartum on the same section as tumor versus no tumor compared to overall average for all postpartum cases analyzed. **D)** Pearson analysis reveals no correlation between proximity to tumor and LVD in postpartum cases, r=0.01296, p=0.69.



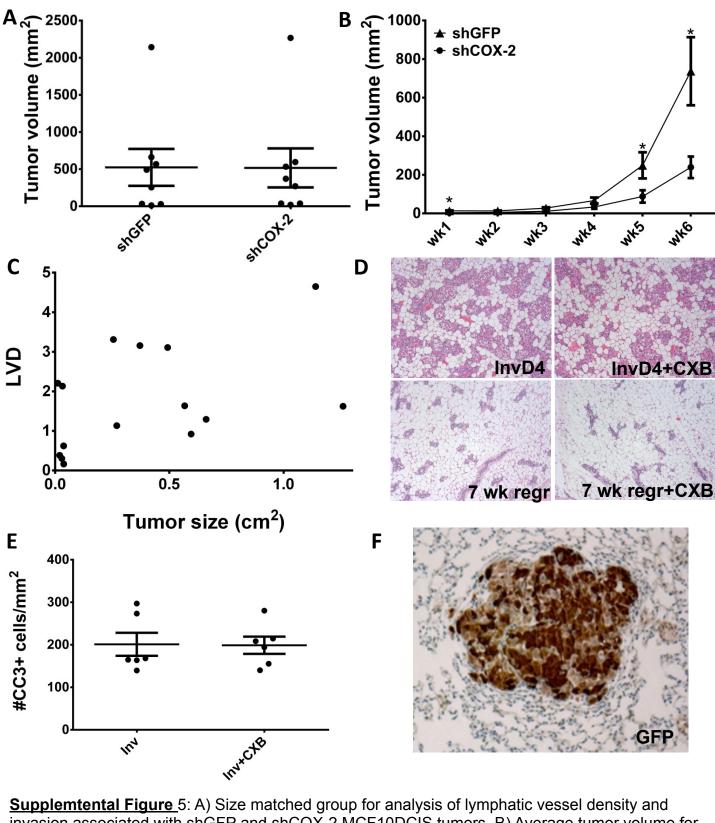
<u>Supplemental Figure 2:</u> A) Lyve-1+ vessels/mm² in mammary tissues from C57/Bl6 mice that were nulliparous (N), pregnant (Pg), Lac (lactating), undergoing involution (InvD1-2, InvD3-4, & InvD6-8), or fully regressed (3 wk regr). B) Lyve-1+ vessels/mm² in mammary tissues from ICR-SCID mice that were nulliparous, or undergoing involution (InvD2 and InvD4), or >4 weeks regressed. C) # lyve-1+ single cells/mm² in rat mammary tissues from nulliparous (N), lactating (Lac), undergoing early involution (InvD2 and InvD4), or fully regressed (R). C) % lyve-1+ vessels containing cells or cellular debris in rat mammary tissues. For each panel all data points, as well as Average and SEM, are depicted.



<u>Supplemtental Figure 3:</u> A) Lyve-1 stained section from a postpartum group animal depicting Lyve-1+ vessel structures (arrows). B) Lyve-1 stained section from a postpartum group animal depicting lymphatic invasion by tumor cells (arrow). For all images T=tumor and PT=peritumor. C) Tumor size at 2, 3, 4, and 5 weeks post-injection when 66cl4 cells are injected into nulliparous or involution day 1 BALB-C dams. D) Tumor size matched group utilized for analysis of # lung clonogenic colonies per animal. E) Average lung micromet size by H&E analysis. F) Average number of lung micromets/animal by H&E analysis.



<u>Supplemtental Figure 4:</u> A) Average number of lymphatic endothelial cells (LECs) migrated to the bottom of a transwell filter toward nulliparous (N) or involution (Inv) tumor cell populations, two-tailed t-test, **p<0.01. B) Representative image of tube formation assay performed in the presence of nulliparous (Nullip) or postpartum (Inv) group tumor cell coniditioned media. Scalebar=100mm. C) Image of tube formation assay stained for VE-cadherin. Scalebar=20mm. D) # cells per field in images taken from proliferation assays in the presence of tumor cell conditioned media. E) Western blot densitometry for COX-2 expression in lysates from nulliparous and involution group tumor cell populations. **p<0.01. t-test.



B < 1000

★ shGFP

invasion associated with shGFP and shCOX-2 MCF10DCIS tumors. B) Average tumor volume for postpartum animals injected with shGFP or shCOX-2 cells during involution. C) Pearson correlation analysis of tumor size and LVD, r=0.4579, n.s. p>0.05. D) H&E stained SCID mouse mammary tissues from Inv4 and 7 week regressed +/- CXB. E) # cleaved caspase 3 positive (CC3+) cells/mm2 in SCID mouse mammary tissues at involution day 4. F) GFP stained tumor cells in mouse lung section (top) and H&E stained section from a postpartum group animal depicting LVI (arrow).