

## SUPPLEMENTAL FIGURE LEGENDS

### Supplemental Figure 1. TAM-derived VEGF-C decreases lung metastases

66cl4 and 4T1 cancer cells were injected into the mammary fat pad of syngeneic mice.

**A-B**, 66cl4 and 4T1 tumor sections were immunostained for CD31 (green), Podoplanin (red) and F4/80 (green) in **(A)**. Graphs depict morphometric analysis of TAMs expressing Podoplanin in **(B)**.

**C**, Graph depicts morphometric analysis of CD31<sup>+</sup> vessel area (%).

**D**, qPCR analysis of VEGF-A gene expression in flow cytometry-sorted TAMs or GFP<sup>+</sup> cancer cells from 4T1 and 66cl4 tumors is depicted in the graph.

**E-F** Representative images for NG2 (green),  $\alpha$ -SMA (red), CD31 (blue) and DAPI (grey) in **(F)**. The graph displays morphometric analysis of pericyte covered blood vessels in **(G)**.

All images are quantified per optic field and bars represent 100  $\mu$ m. Statistical analyses were performed by Students t-test for **(A)**, one-way ANOVA in **(C)** and by \* indicates significance; \* $p < 0.05$ ; \*\* $p < 0.01$  \*\*\* $p < 0.001$   $n > 10$ . Bars represent 100  $\mu$ m. All data are presented as the mean + SD.

### Supplemental Figure 2. VEGF-C integration levels and protein expression in hemopoietic cells

4T1 tumor cells were injected into the mammary fat pad of syngeneic chimeric mice harboring haemopoietic cells engineered to express VEGF-C or only the lentiviral backbone (CTRs).

**A**, Schematics describing the experimental procedure.

**B**, Genomic DNA was analyzed by qPCR for lentiviral integration of VEGF-C in bone marrow stem cells from CTR and VEGF-C chimeric mice. Histogram depicts lentiviral copies normalized to  $\beta$ -actin.

**C**, VEGF-C protein expression in BMDMs derived from CTR and VEGF-C chimeric mice was analyzed by western blot.

**D**, RT-PCR analysis of VEGF-A gene expression in BMDMs attained from CTR and VEGF-C chimeric mice.

**E**, The histogram depicts CTR and VEGF-C tumor weight (g).

**F-H**, Representative images show immunofluorescence staining of tumor sections from CTR and VEGF-C chimeric mice for CD31 (green), Podoplanin (red) and F4/80 (green). Graph depicts morphometric analysis of lymphatic vessels in **(G)** and CD31 tumor vessel number in **(H)**.

All images are quantified per optic field and bars represent 100  $\mu$ m. Statistical analyses were performed by Students t-test, \*indicates significance; \* $p < 0.05$ ; \*\*\*\* $p < 0.001$ ,  $n > 15$ . All data are presented as the mean + SD.

### **Supplemental Figure 3. TAM-derived VEGF-C decreases vessel permeability**

4T1 cancer cells were co-mingled in matrigel with BMDMs transduced with CTR or VEGF-C LVs and injected subcutaneously into syngeneic mice.

**A**, Schematic figure of the co-mingling assay

**B**, CTR and VEGF-C tumor sections were immunostained for CD31 (green), biotin conjugated dextran (red). Bars represent 100  $\mu$ m. Vessel leakage is defined as extravasating dextran as visualized in the graph ( $n = 5$ ; \*\*\*\* $p < 0.0001$  \* indicates significance by students t-test).

### **Supplemental Figure 4. TAM-derived VEGF-C does not affect myeloid and lymphoid immune landscape**

**A-F**. Graphs show flow cytometry analysis of 4T1-CTR and 4T1-VEGF-C tumors for myeloid cells in **(A)**, TAMs in **(B)**, neutrophils in **(C)**, immunoactivating TAMs in **(E)**, immunosuppressive TAMs in **(F)**.

**G**, Graph displays quantitative RT-PCR analysis of gene expression levels of CTR and VEGF-C transduced BMDMs. Gene expression was normalized to  $\beta$ -actin levels.

**H**, Flow cytometry analysis of 4T1-CTR and 4T1-VEGF-C tumors for T cells and NK cells.

All statistical analyses were performed by Students t-test, and was not significant,  $n > 15$ . All data represents are presented as the mean + SD.

### **Supplemental Figure 5. Vessel number is not changed with malignant BC grade**

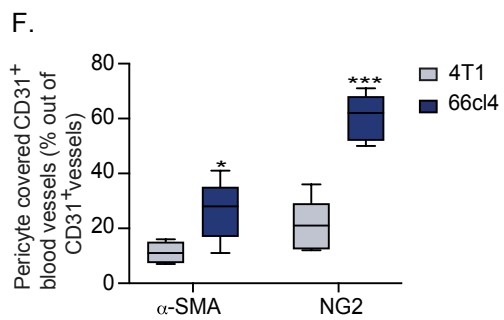
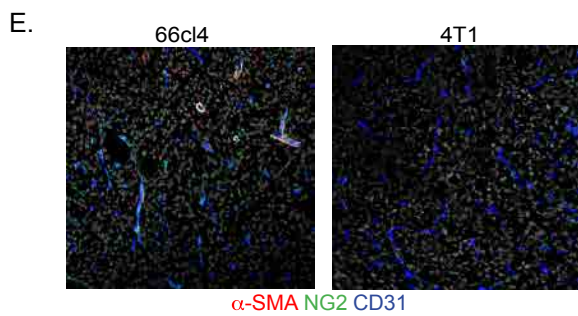
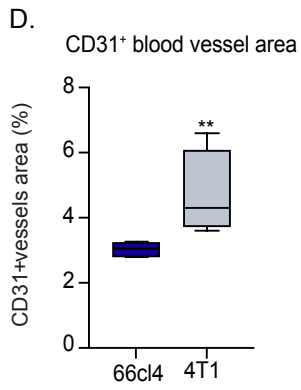
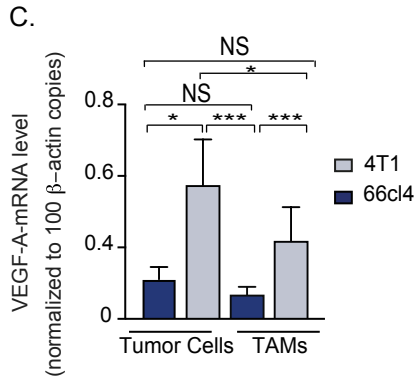
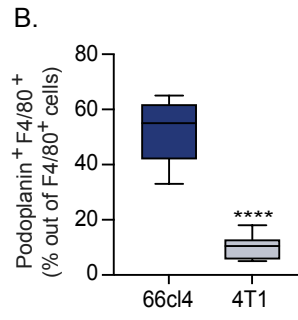
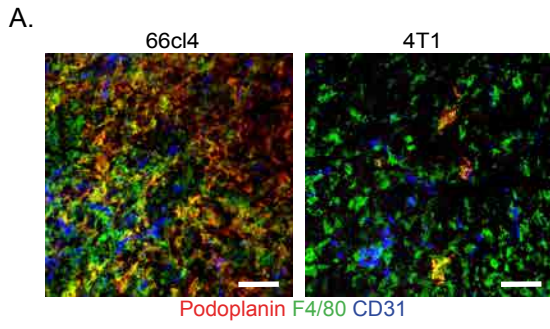
The graph depicts morphometric analysis of BC specimens of grades II and III immunostained for CD31,  $n > 4-16$ . Statistical analysis by students t-test was not significant (NS).

### **Supplemental Figure 6. Tumor cell-derived VEGF-C does not affect tumor weight**

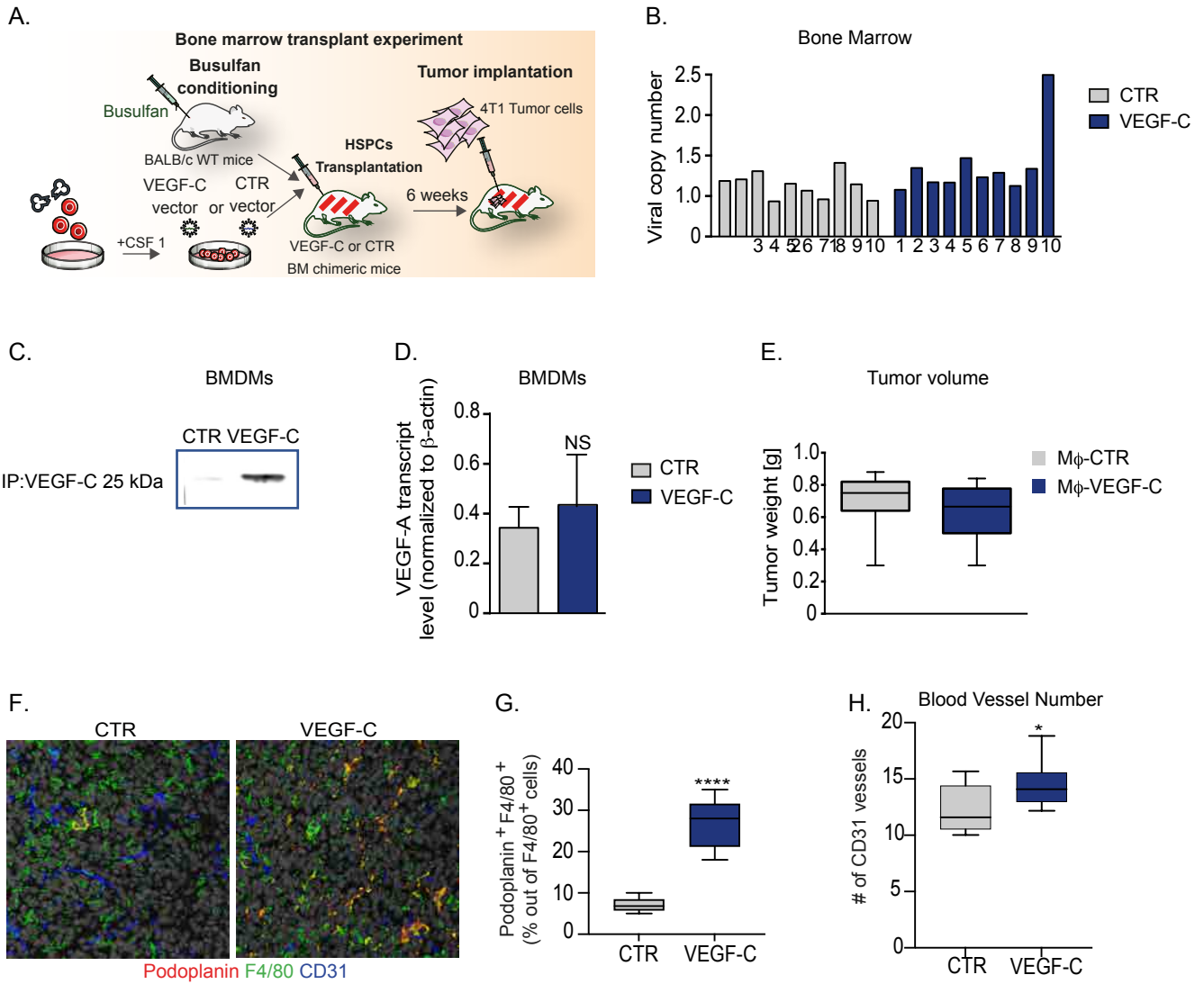
4T1-CTR and 4T1-VEGF-tumor cells were inoculated into the fat pad of syngeneic mice.

**(A)** Graph depicts tumor weight ( $n = 5$ ).

# Supplemental Figure 1

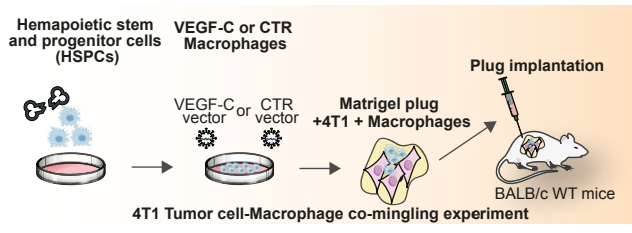


## Supplemental Figure 2

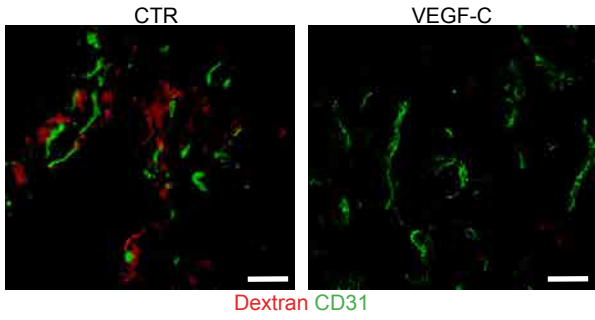


### Supplemental Figure 3

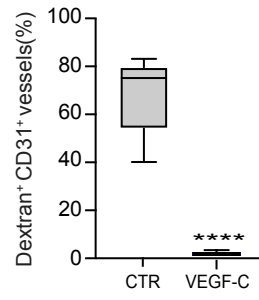
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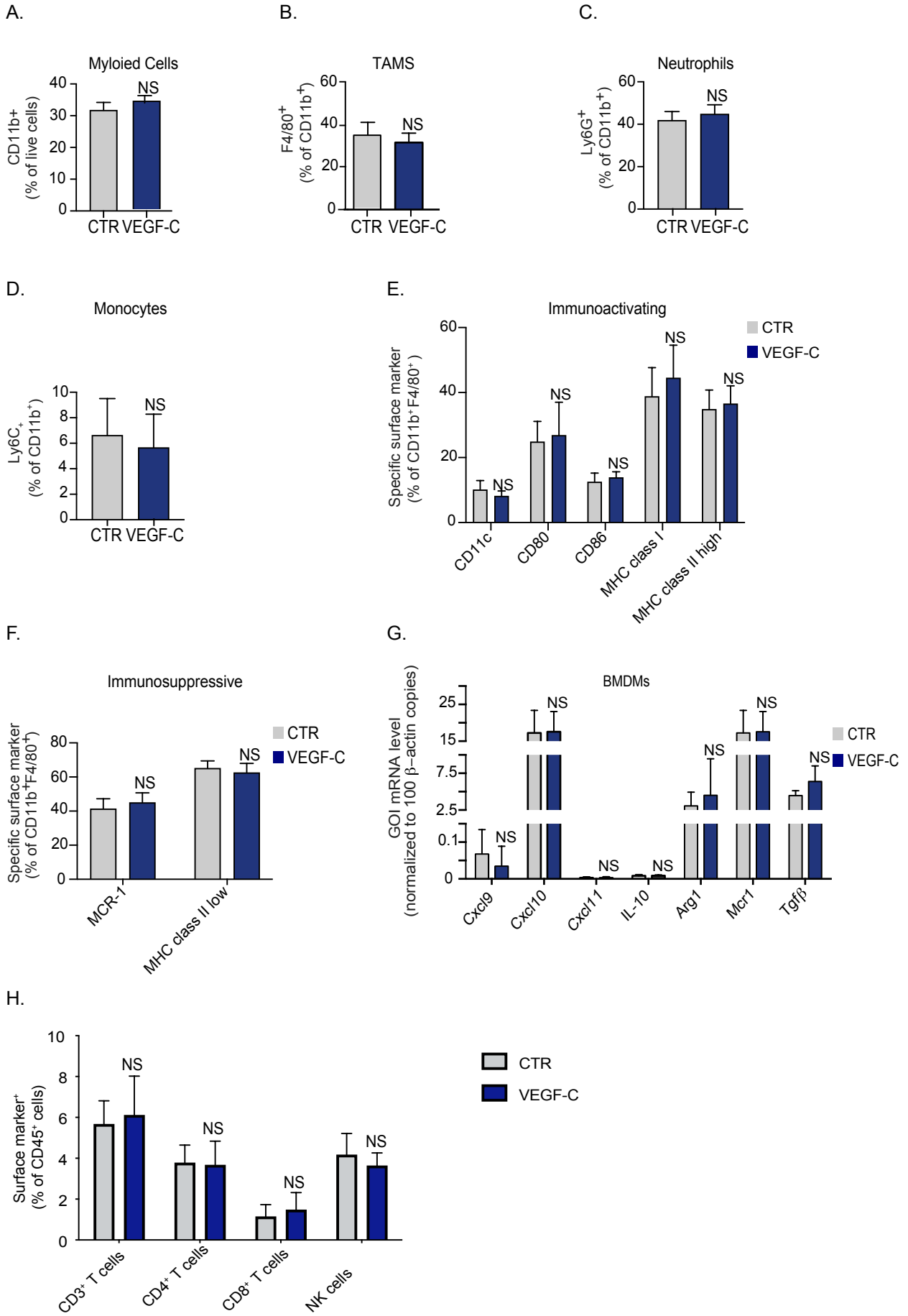
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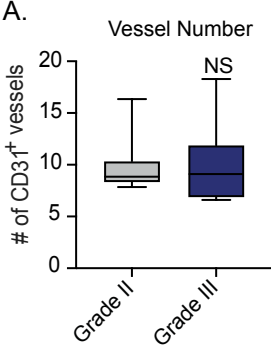
C.



# Supplemental Figure 4



Supplemental Figure 5



**Supplemental Figure 6**

A.

