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Crosstalk between osteoblasts and breast cancer cells alters breast cancer proliferation through multiple mechanisms

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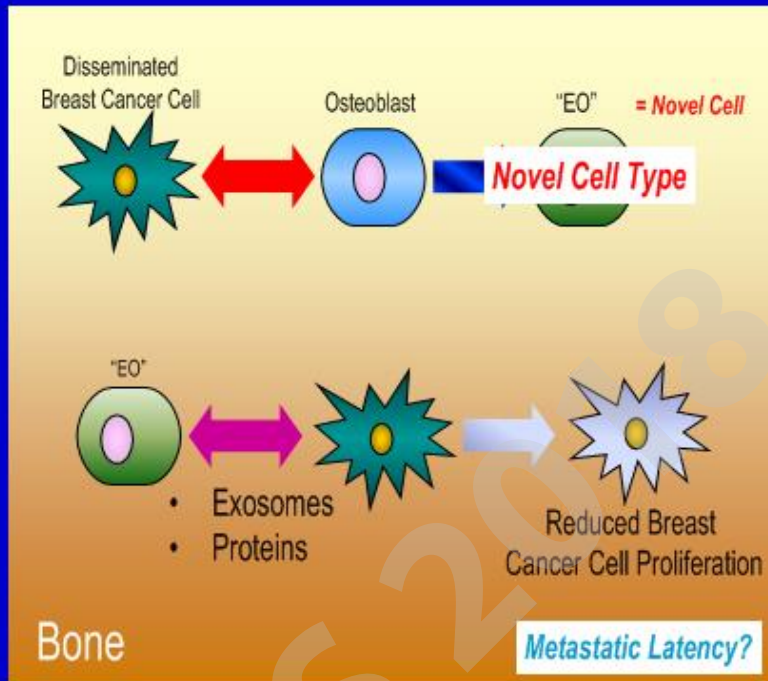
Breast Cancer Metastases to the Bone

- Bone microenvironment provides a fertile soil for metastatic breast cancer cells
- Cancer cells may manipulate cells of the bone, such as osteoblasts, to influence metastatic progression



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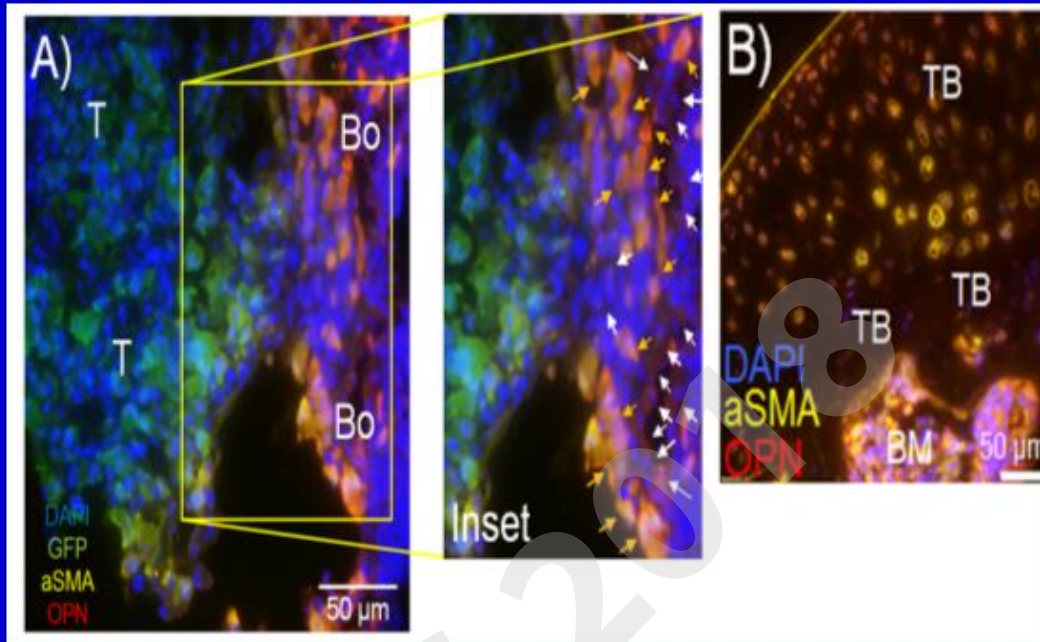
EOs Suppress Breast Cancer Cell Proliferation



Objective

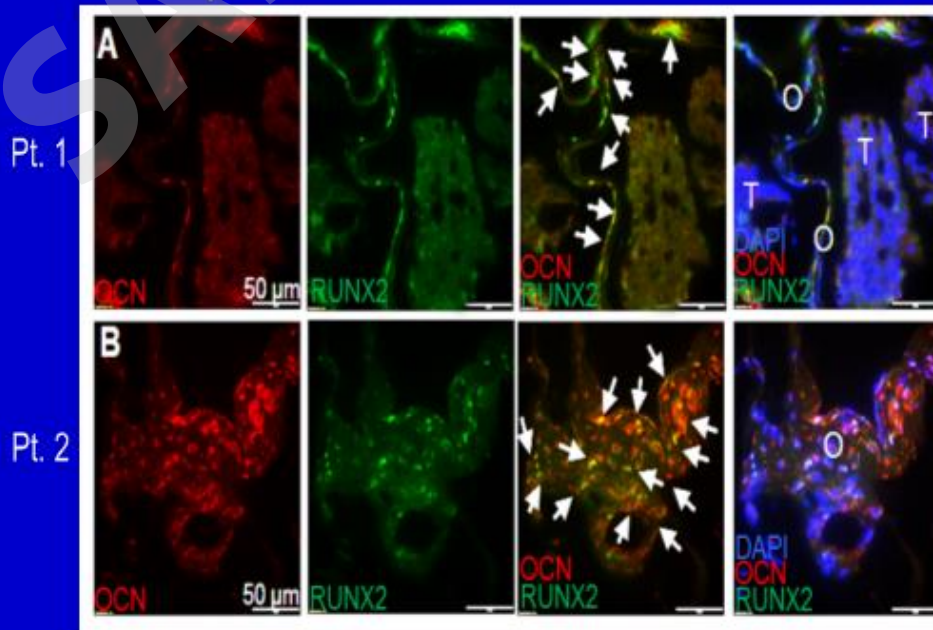
- Analyze mechanisms of crosstalk between osteoblasts and breast cancer cells that alter breast cancer cell proliferation

Two subpopulations of osteoblasts are present in the bones of tumor-bearing mice



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Osteoblasts are distinguishable in patient samples of bone metastatic breast cancer

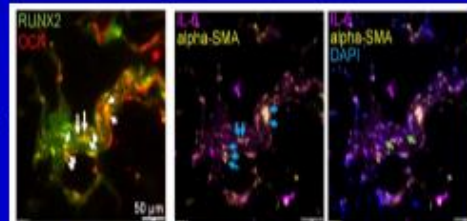


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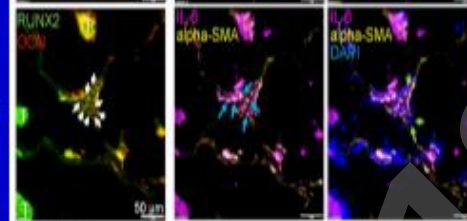
'Educated' Osteoblasts are present in patient samples of bone metastatic breast cancer

Biomarkers	OB	EO
RUNX2	+	+
OCN	+	+
OPN	+	+
alpha-SMA	+	-
IL-6	+	-

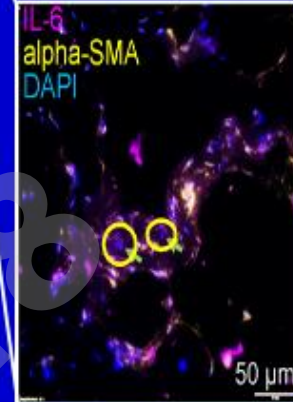
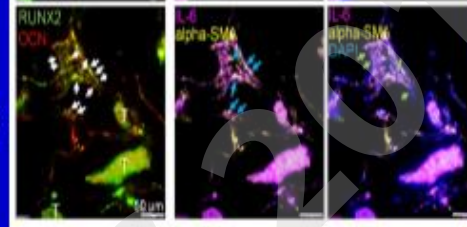
Pt. 1



Pt. 2



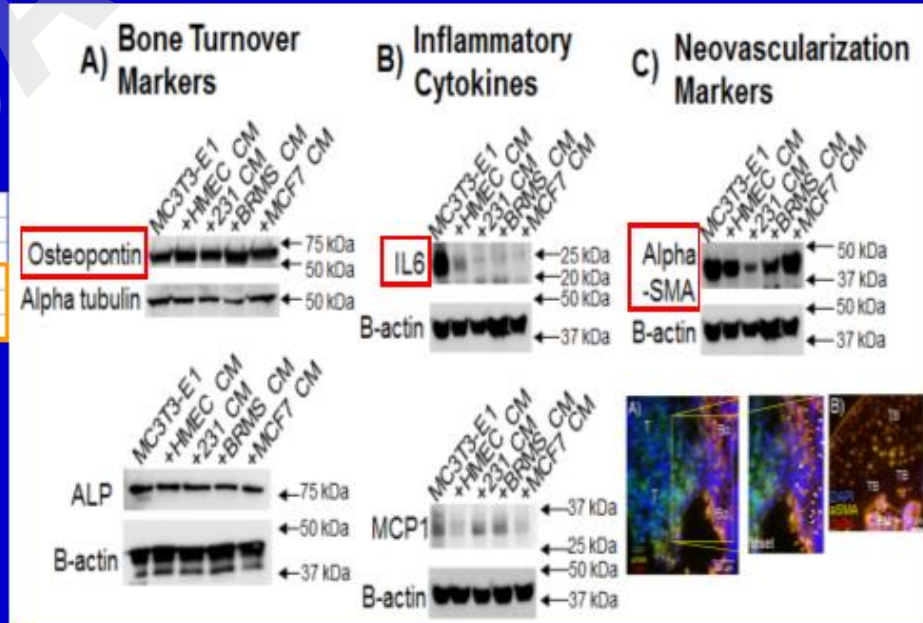
Pt. 3



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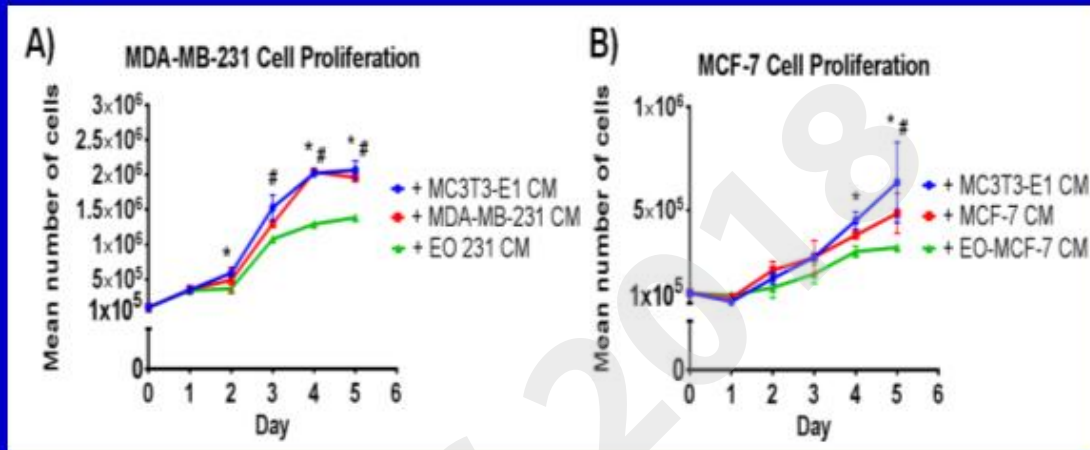
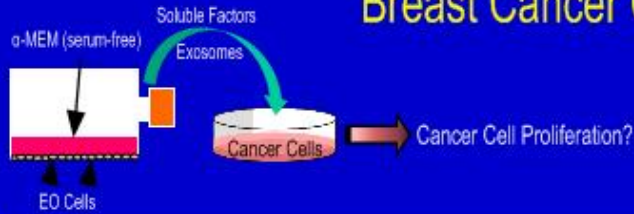
Protein Alterations Distinguish EOs from Naïve Osteoblasts

Biomarkers	OB	EO
RUNX2	+	+
OCN	+	+
OPN	+	+
alpha-SMA	+	-
IL-6	+	-



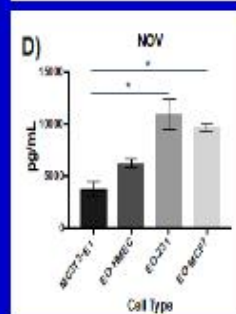
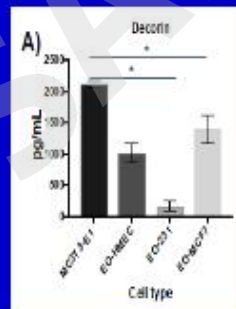
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Conditioned Medium from EOs Decreases Breast Cancer Cell Proliferation



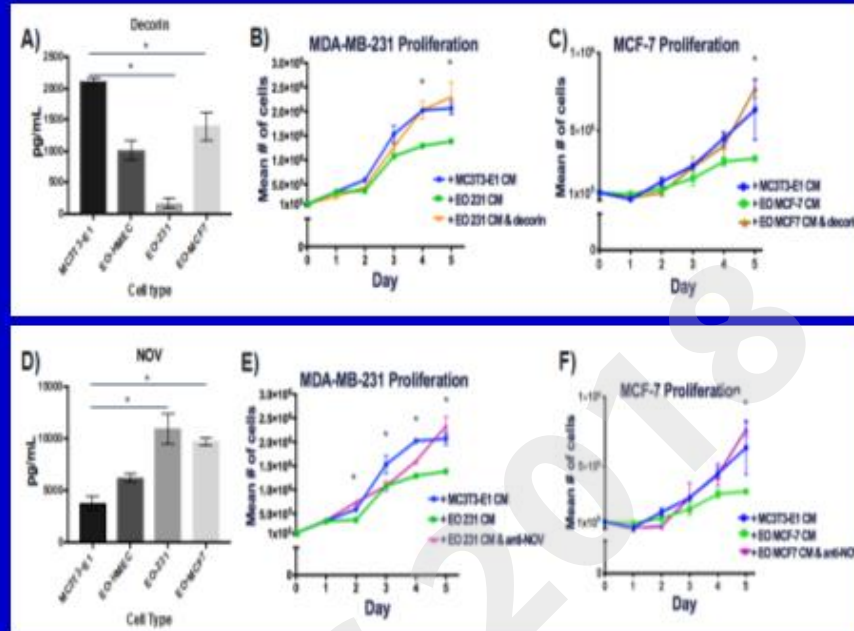
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EO-derived Soluble Factors Modulate Breast Cancer Cell Proliferation



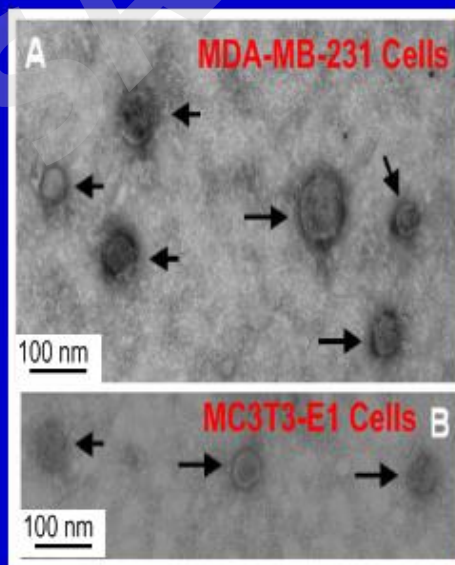
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EO-derived Soluble Factors Modulate Breast Cancer Cell Proliferation



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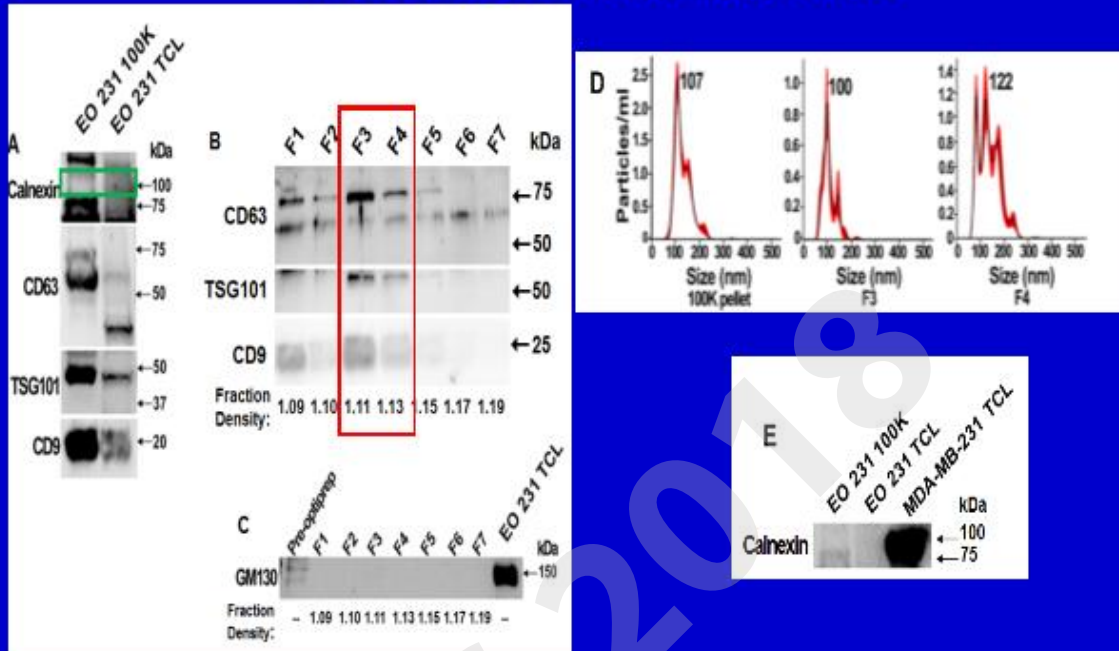
Osteoblasts and Breast Cancer Cells Produce Exosomes



- Vesicles produced by cells
- ~30-150 nm in diameter
- Contain molecular constituents of their cell of origin, including proteins and RNA
- Play a role in cell-to-cell signaling, influencing processes in the recipient cell

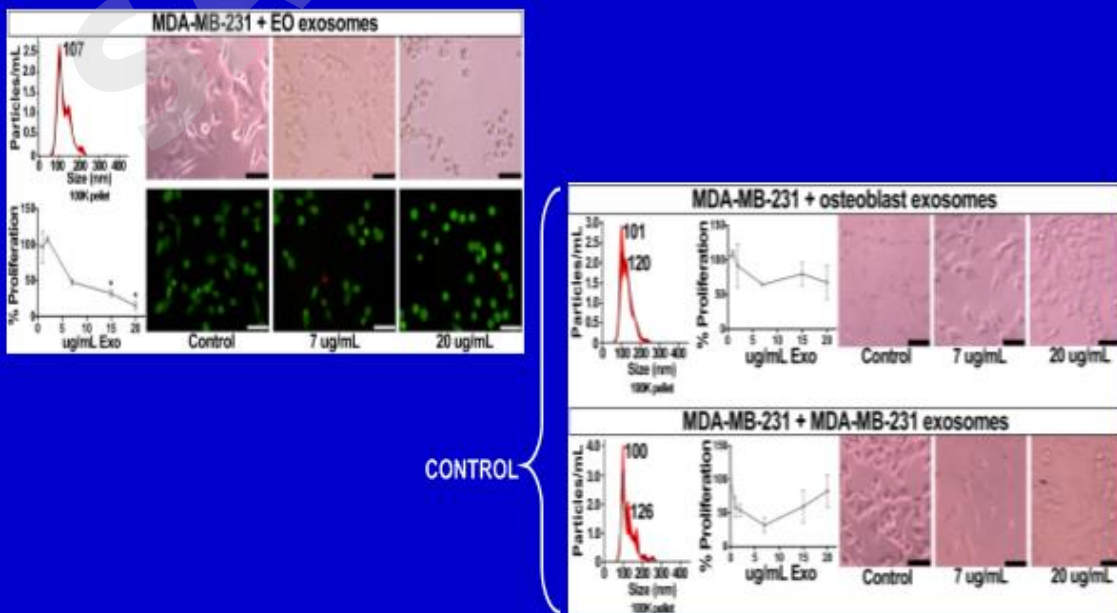
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EO Conditioned Medium is a Rich Source of Exosomes



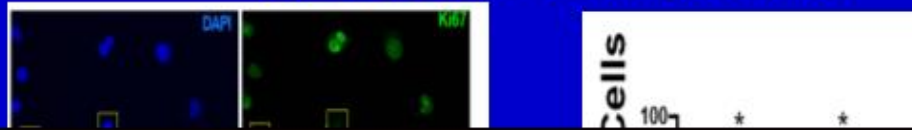
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EO-Derived Exosomes Decrease Triple Negative Breast Cancer Cell Proliferation



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EO-Derived Exosomes Decrease Triple Negative Breast Cancer Cell Proliferation

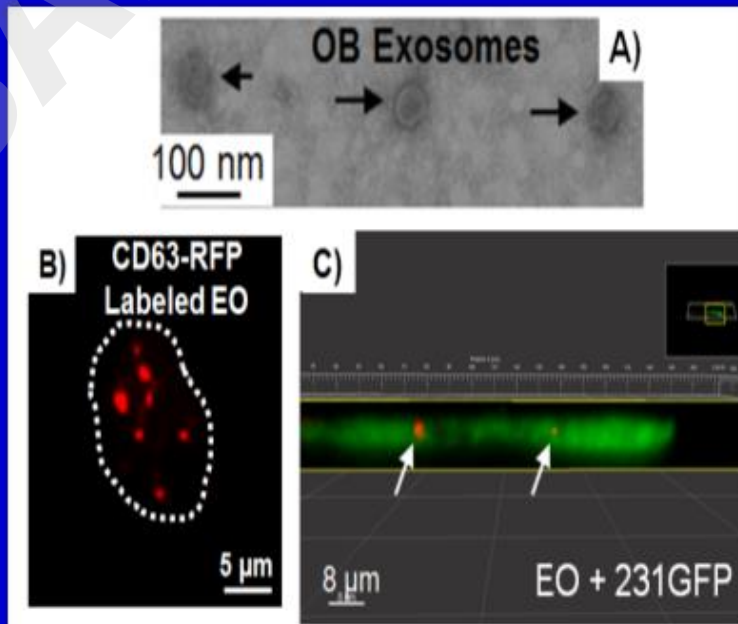


➤ Similar Response with ER+ Breast Cancer Cells



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Breast Cancer Cells take up EO-derived Exosomes



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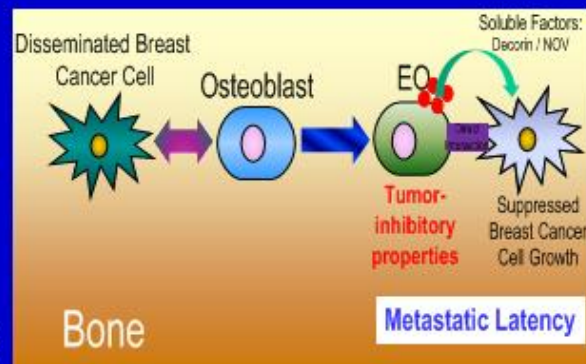
Breast Cancer p21 Expression is Increased in Co-cultures with EOs

➤ **No Significant Differences in Breast Cancer Cell Migration or Invasion**

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Conclusions

- A subpopulation of osteoblasts are altered in the tumor niche in both murine and human samples
- EOs express different proteins than naïve osteoblasts
- Exposure to EO conditioned medium or exosomes reduces triple negative and ER+ breast cancer proliferation *in vitro*
- Co-culture with EOs increases p21 expression in triple negative and ER+ breast cancer cells



➤ **EOs have tumor-inhibitory properties**

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