A Role of Maspin in Prostate Epithelial Homeostasis and Tumor Progression

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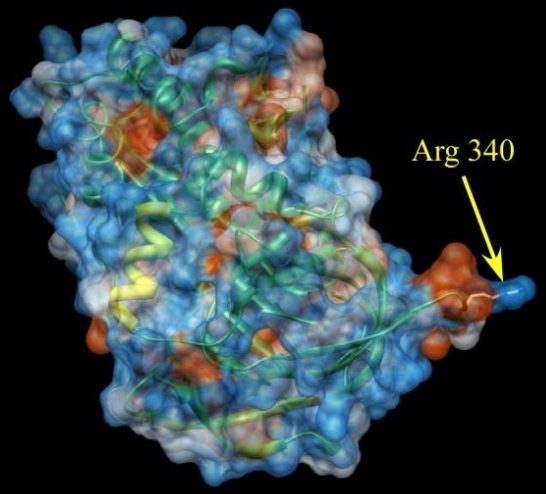
The Sheng Lab:

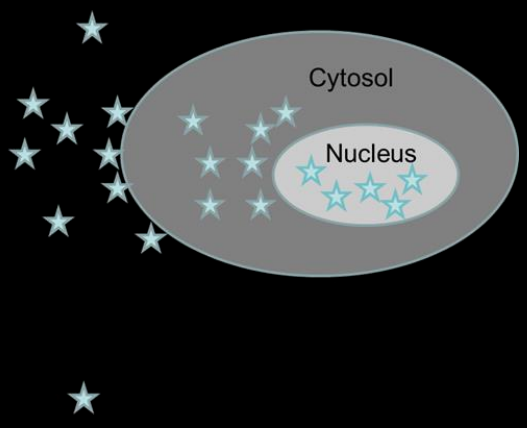
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Epithelial-specific Maspin





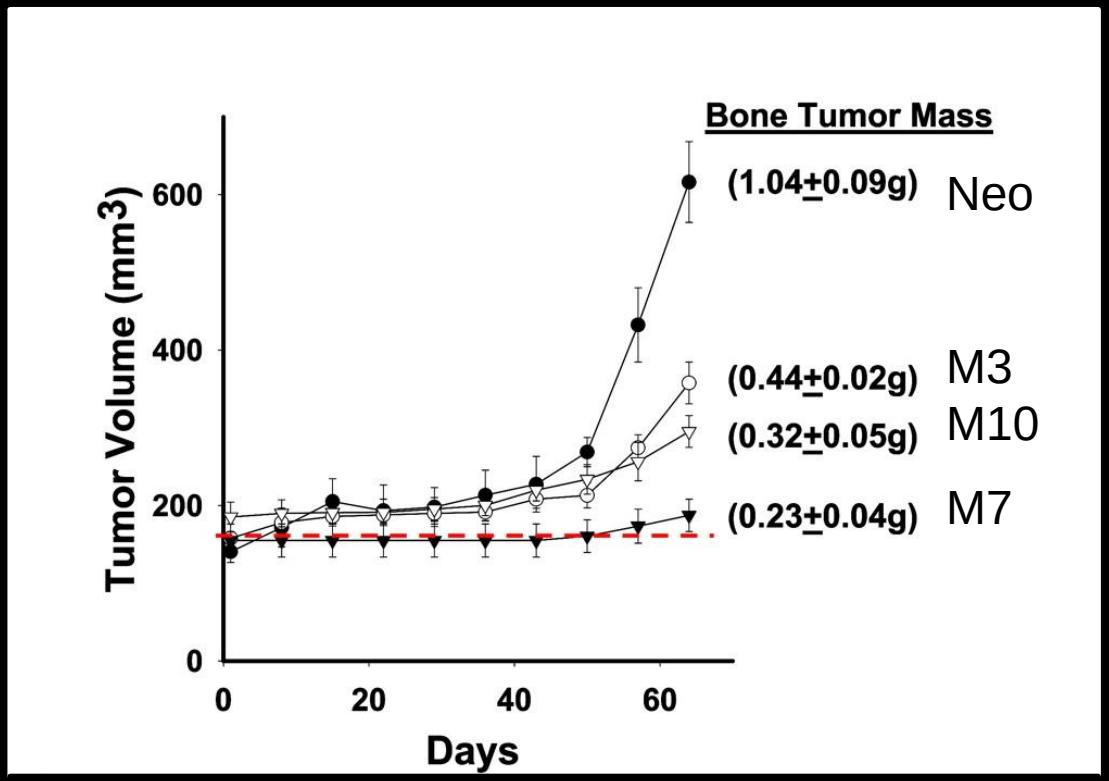
Experimental model:
Prostate cancer bone metastasis
Immune response to tumor xenograft

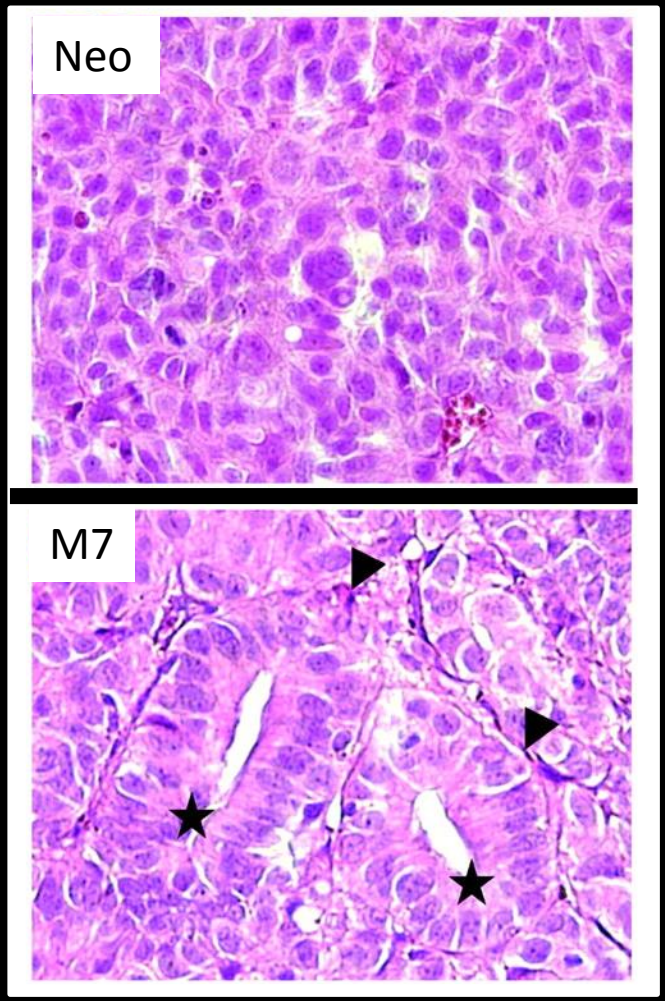
Function:
Limiting microenvironment-induced tumor cell phenotypical plasticity
Increase host immune response

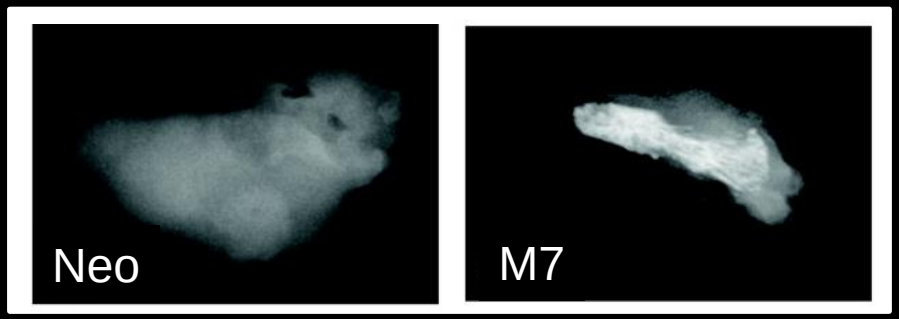
Underlying Molecular Mechanism:
Endogenous HDAC inhibition

Potential Clinical Utility:
Molecular Marker
Maspin-based therapeutic strategy

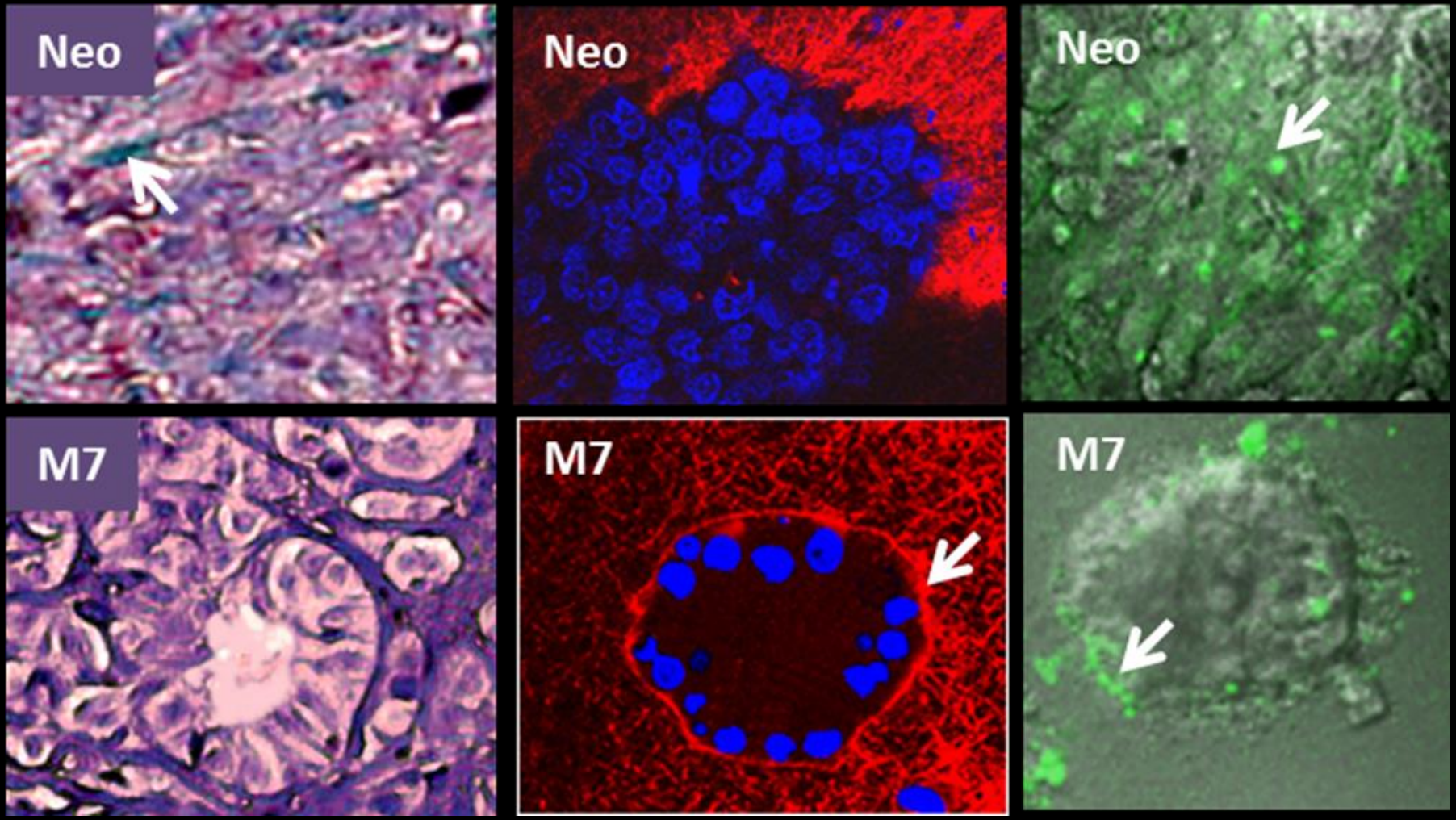
Maspin expression inhibits osteolysis, tumor growth, and angiogenesis in a model of prostate cancer bone metastasis



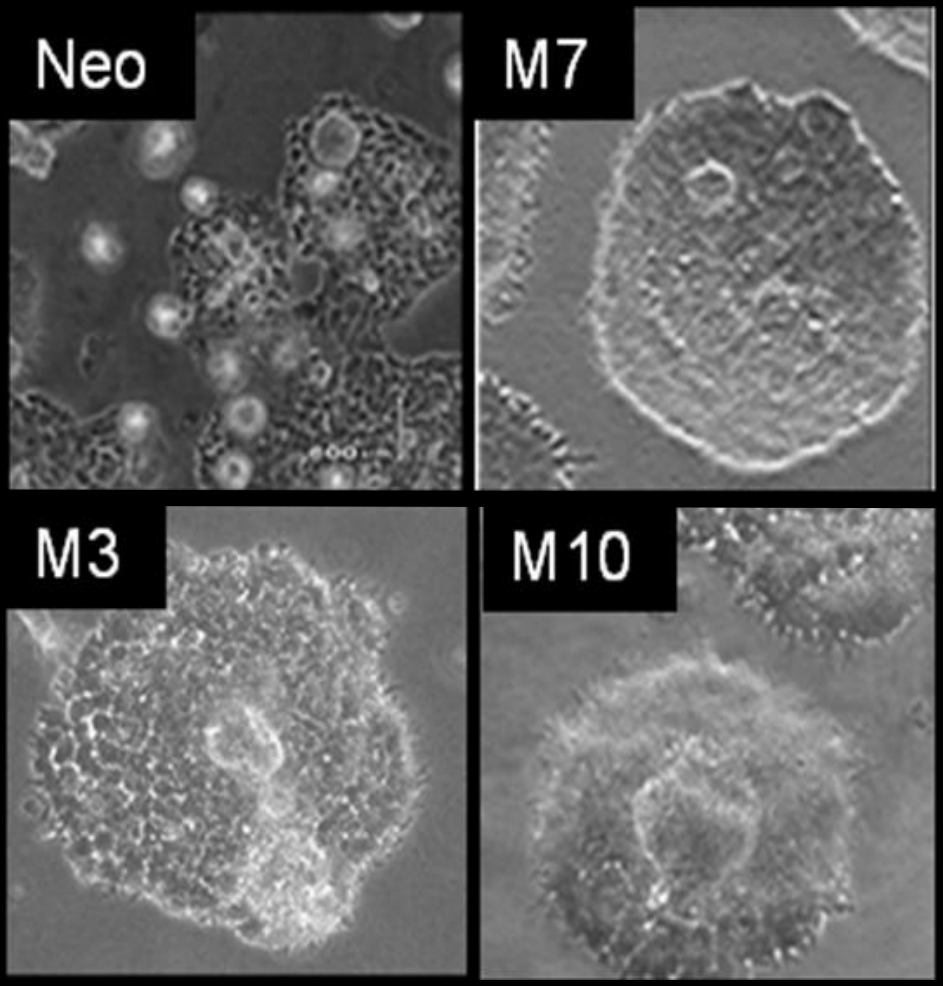


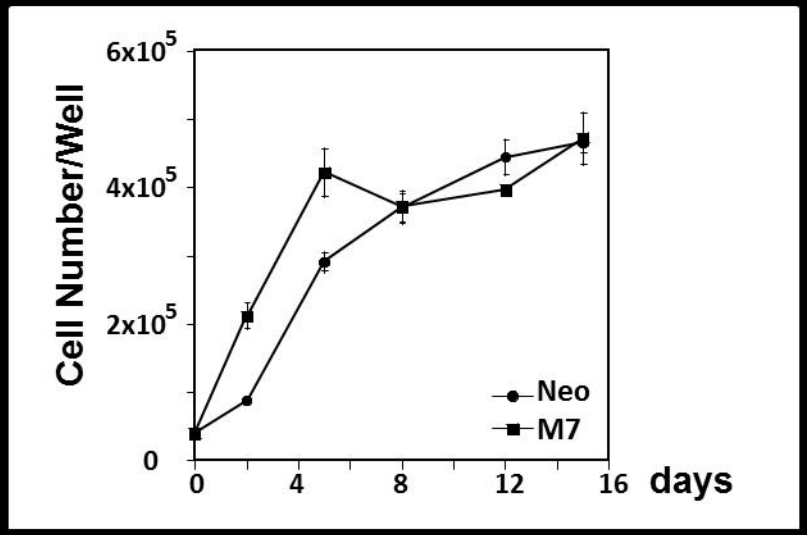


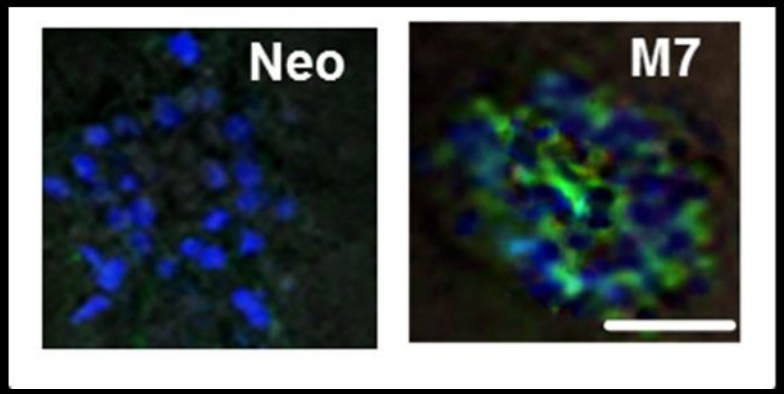
Maspin Reprograms Prostate Cancer Cells toward Differentiation in vivo and in 3D Culture



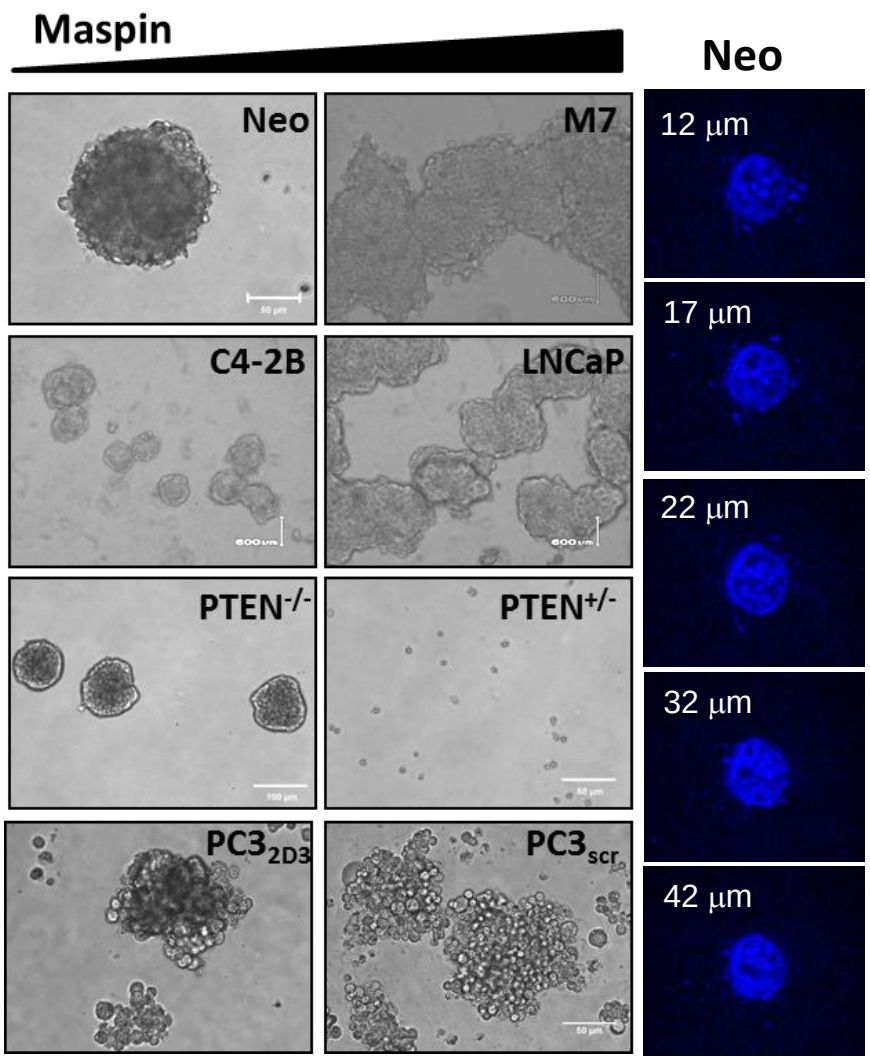
Maspin Reprograms Prostate Cancer Cells toward Differentiation in vivo and in 3D Culture



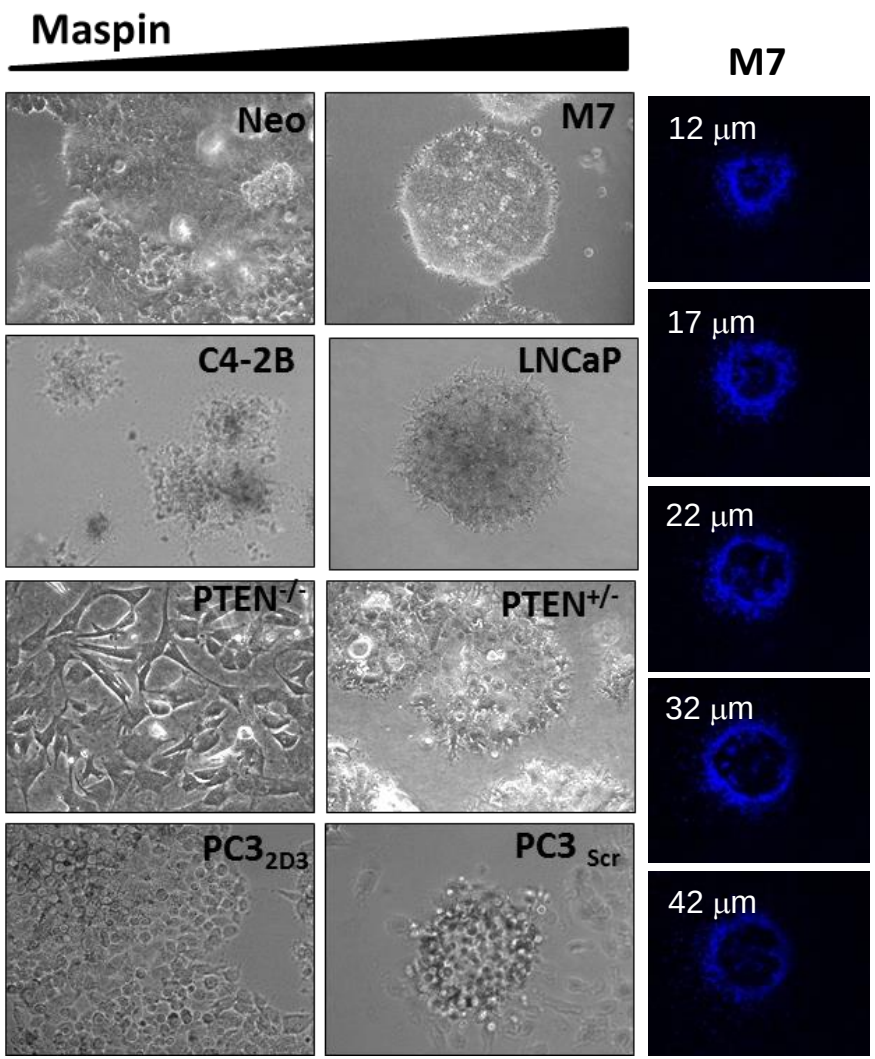




Maspin Correlates with Restriction of "Stemness"



Suspension



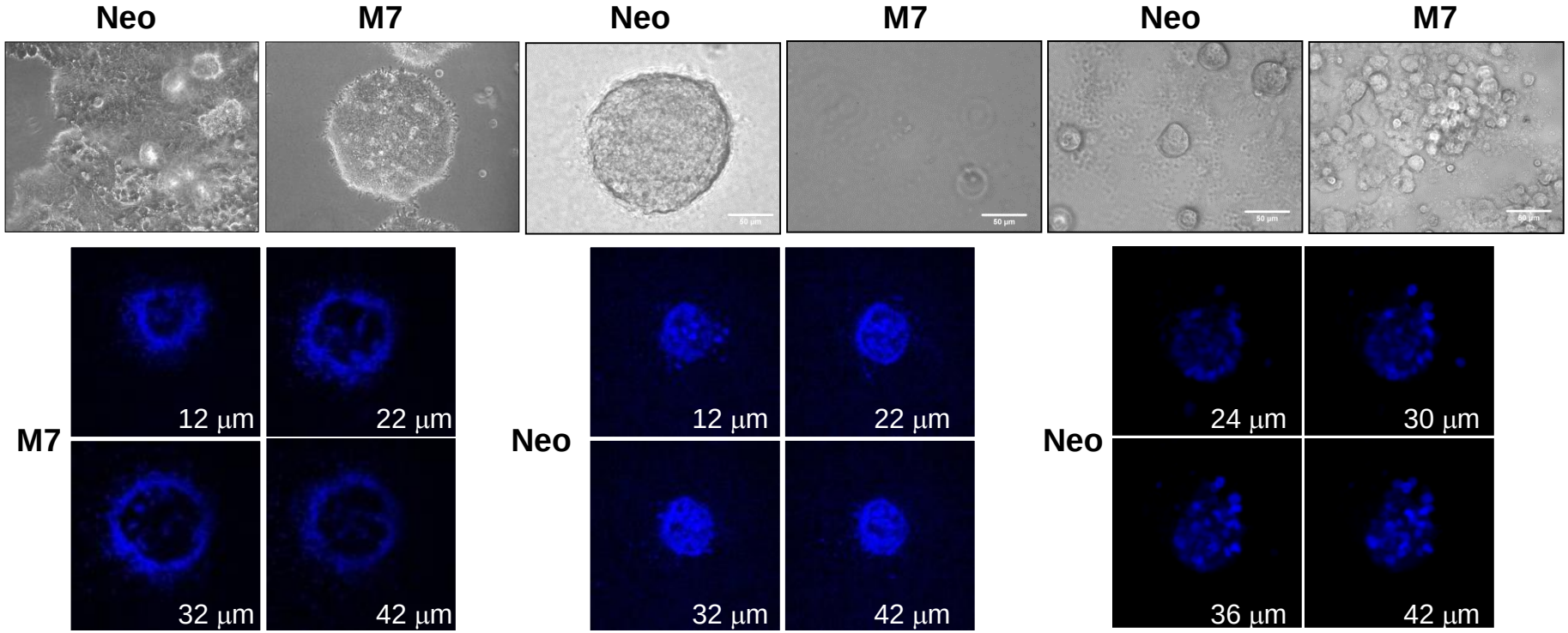
3D in Collagen I

Tumorspheres derived from maspin transfected DU145 cells lost the ability to form epithelial-structures in 3D Col I

Original Cells in 2D → **Embedded in 3D Col I**

Grown in Suspension → **Embedded in 3D Col I**

Grown in Suspension → **Embedded in 3D Matrigel**



Maspin Reduced Stem Cell Marker Expression and Tumor Initiation

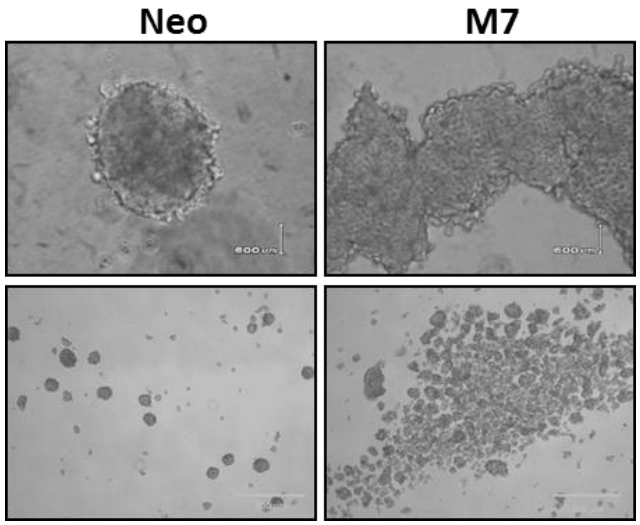
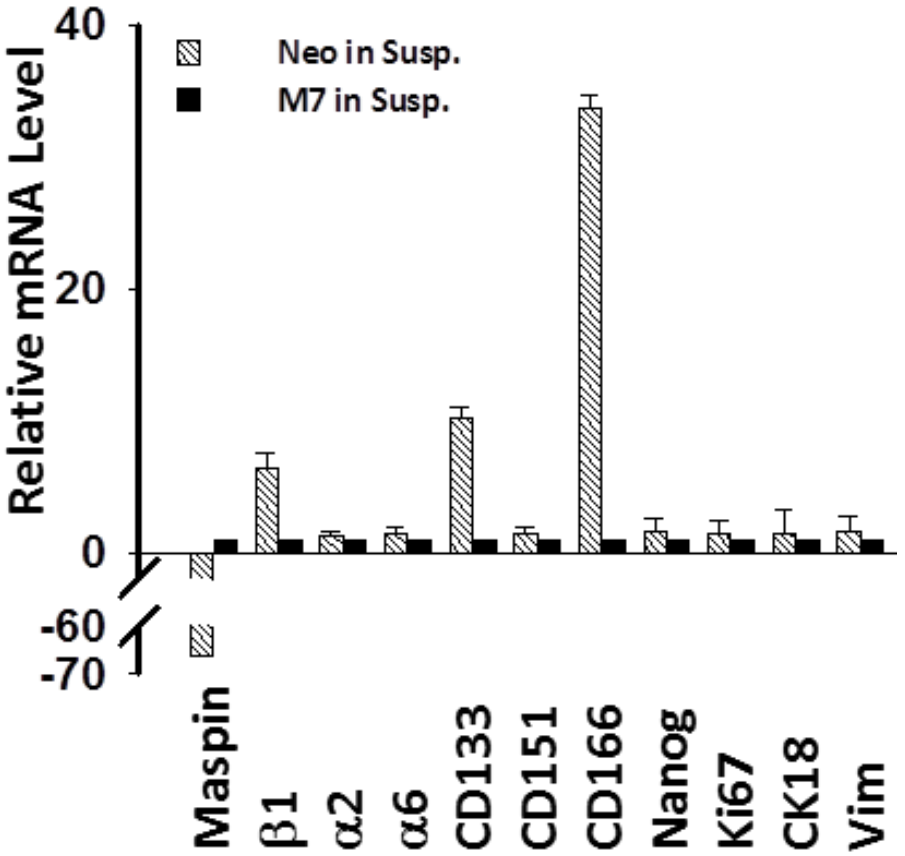
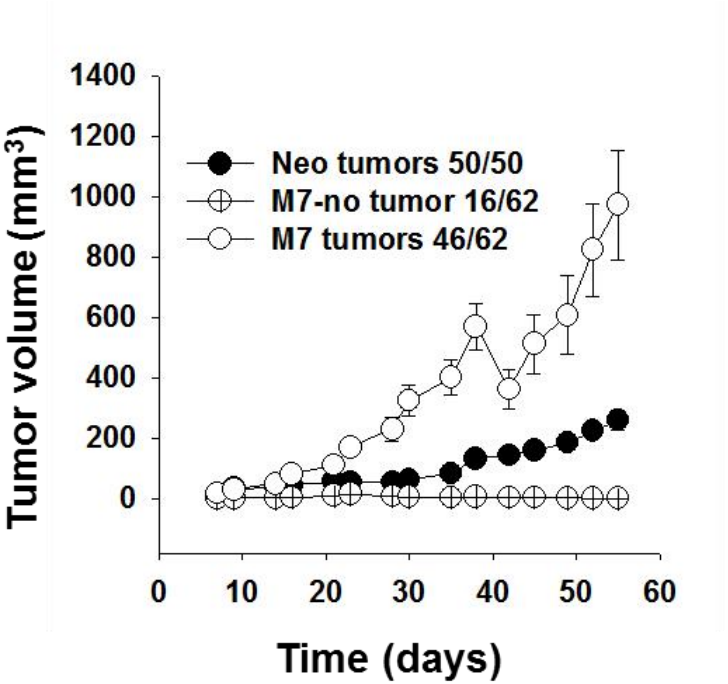


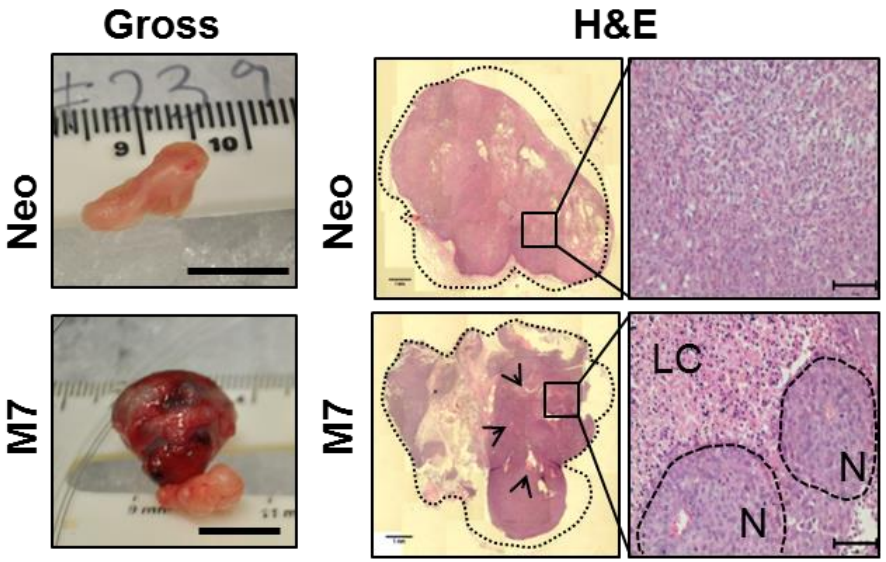
Table I, *In vivo* Tumor Incidence

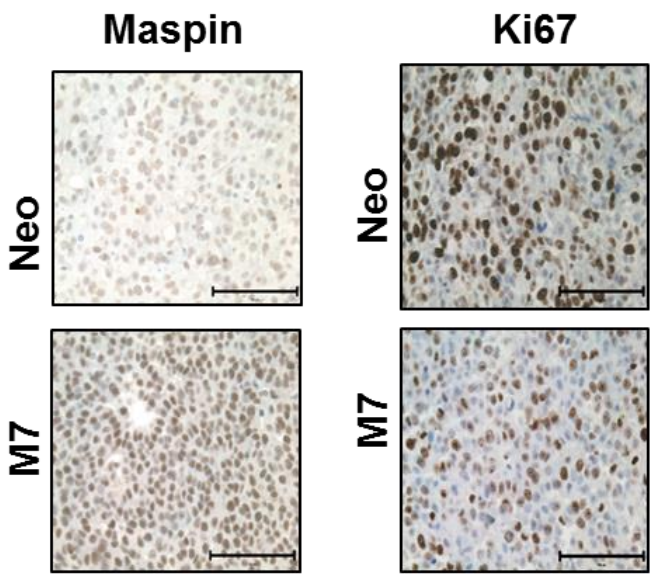
Injected Cells	Neo	M7
50,000	2/6	0/6
10,000	0/6	0/6
5,000	0/6	0/6

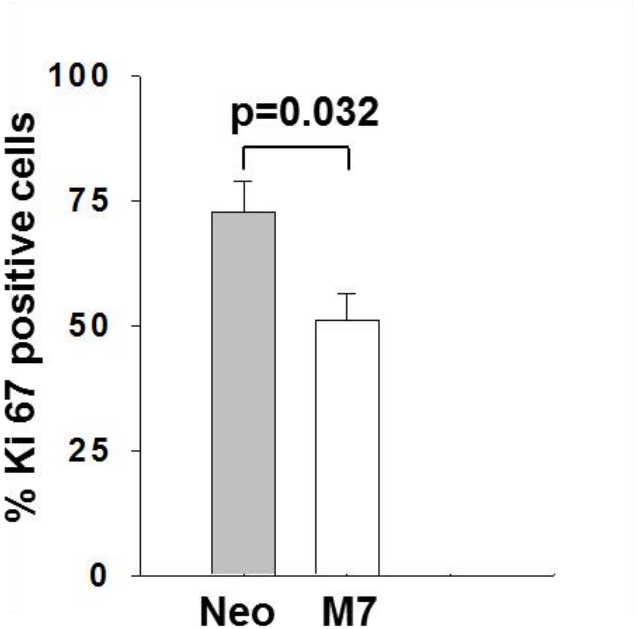


Maspin-expressing xenograft tumors with anti-tumor immune response

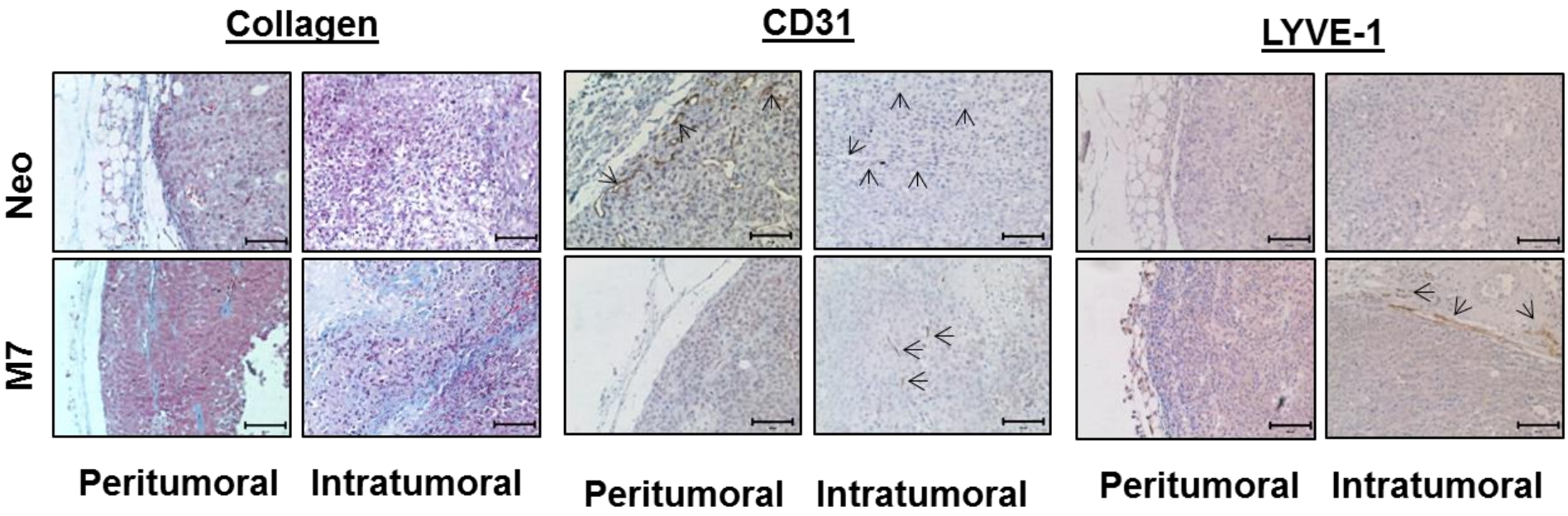




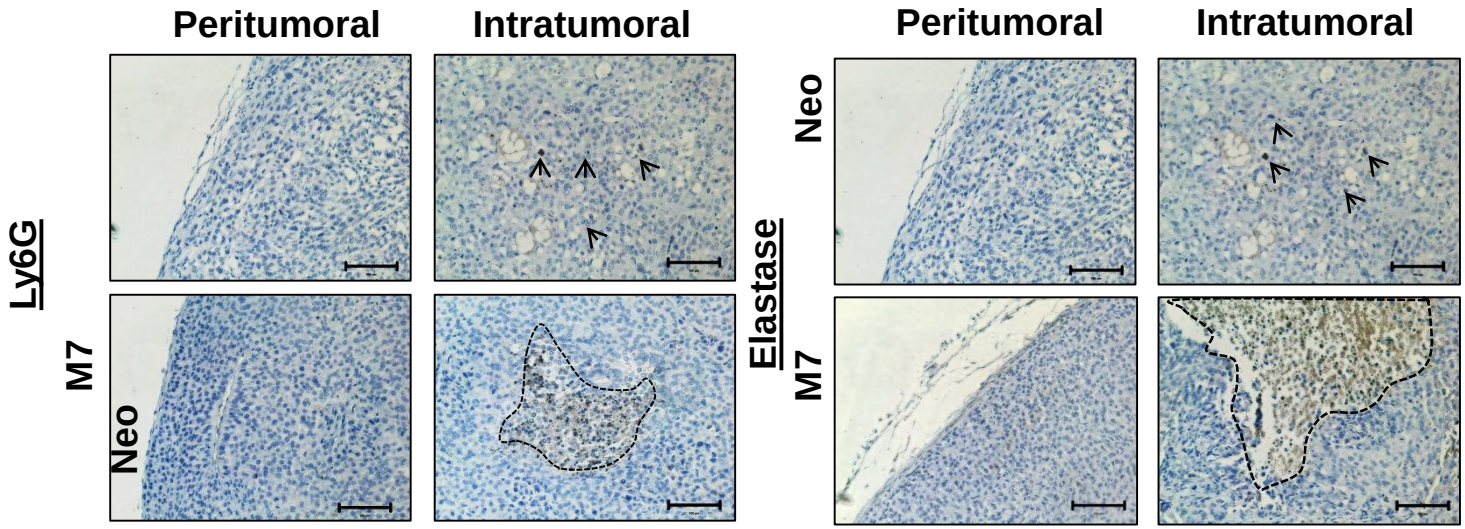


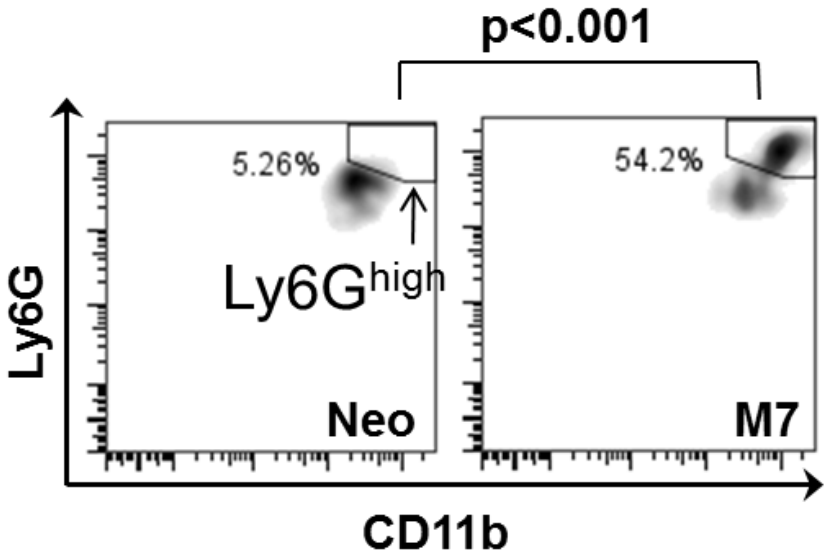


Stromal Response Regulated by Maspin

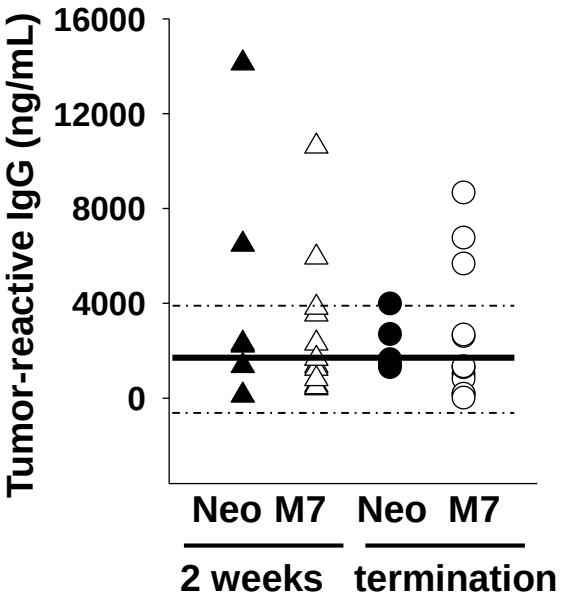


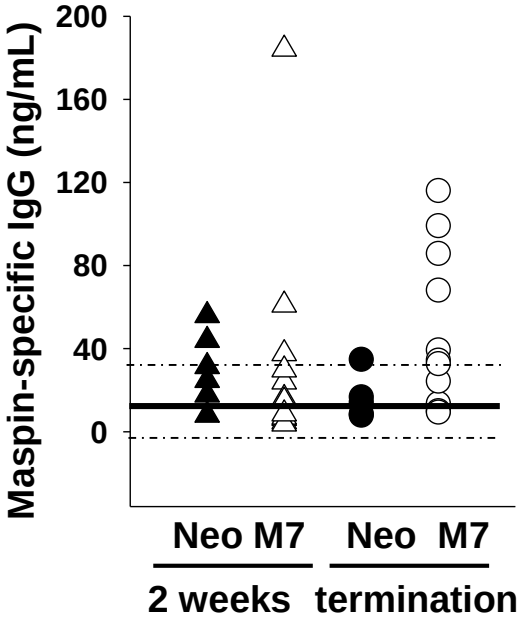
Maspin expression in tumor cells increased neutrophil activation



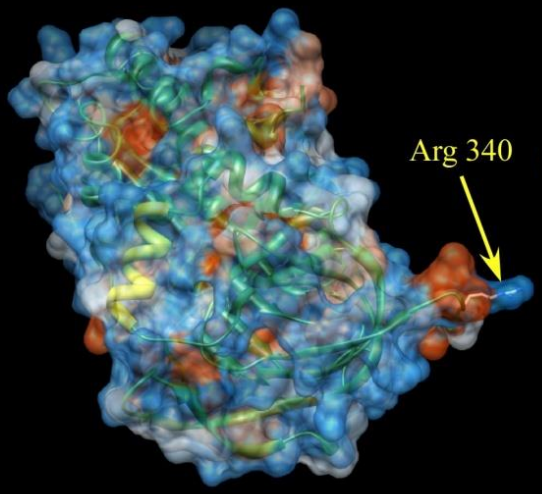


Quantification of tumor-reactive and maspin-specific IgG.

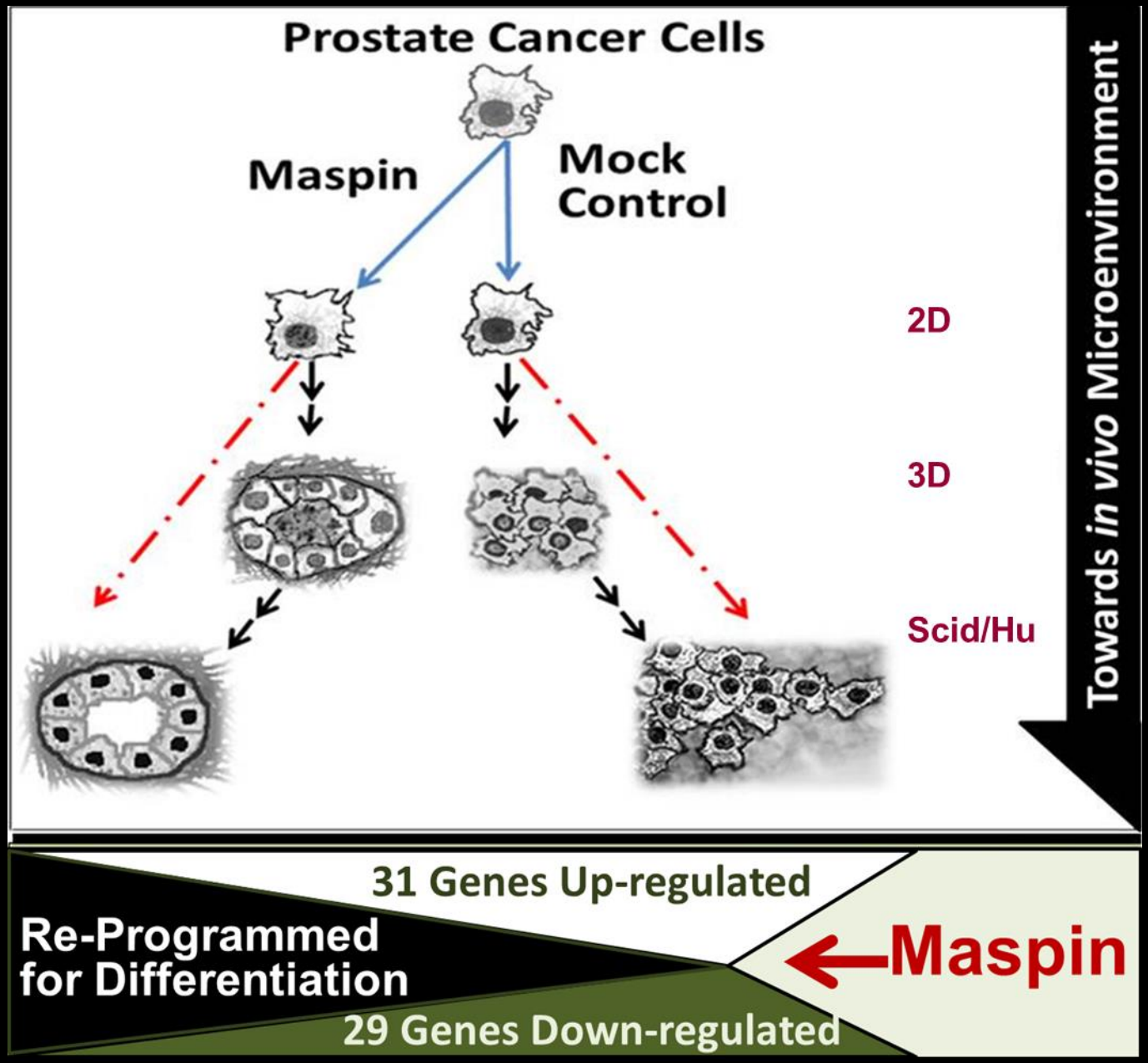




Maspin, an endogenous HDAC1 Inhibitor

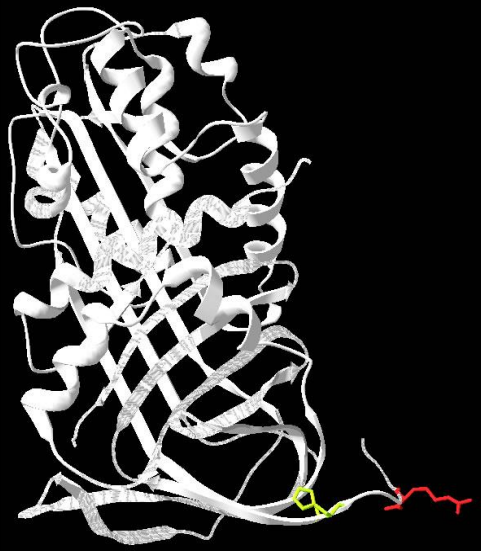


Maspin expression is a fateful step in epithelial cell biology



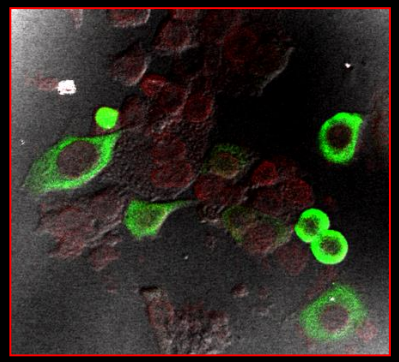


A Control Button for Maspin Translocation- Dzinic S, et al, Plos One, 2013

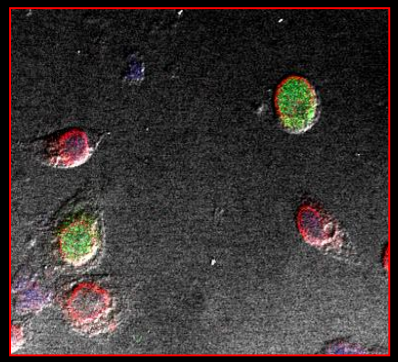




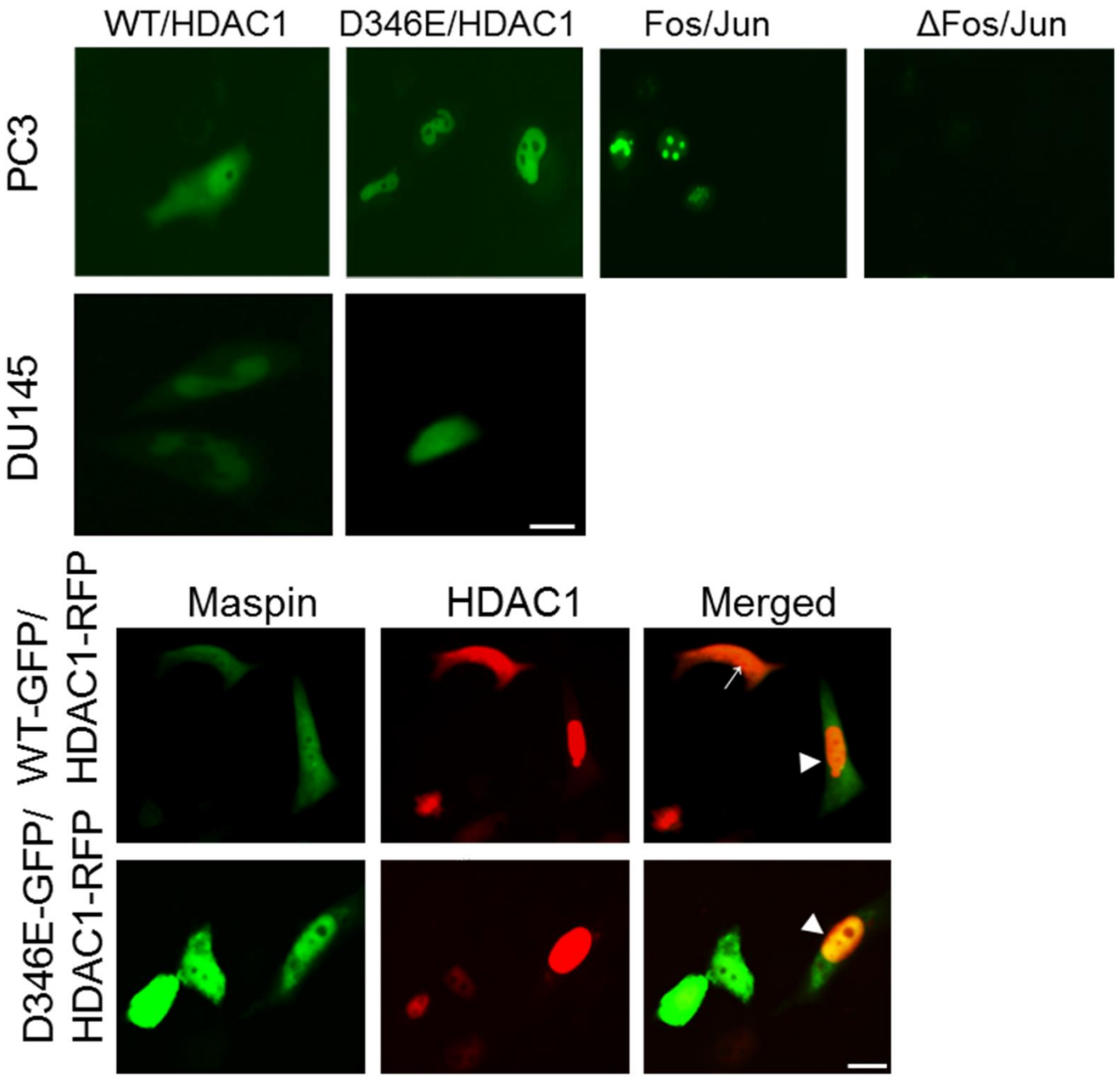




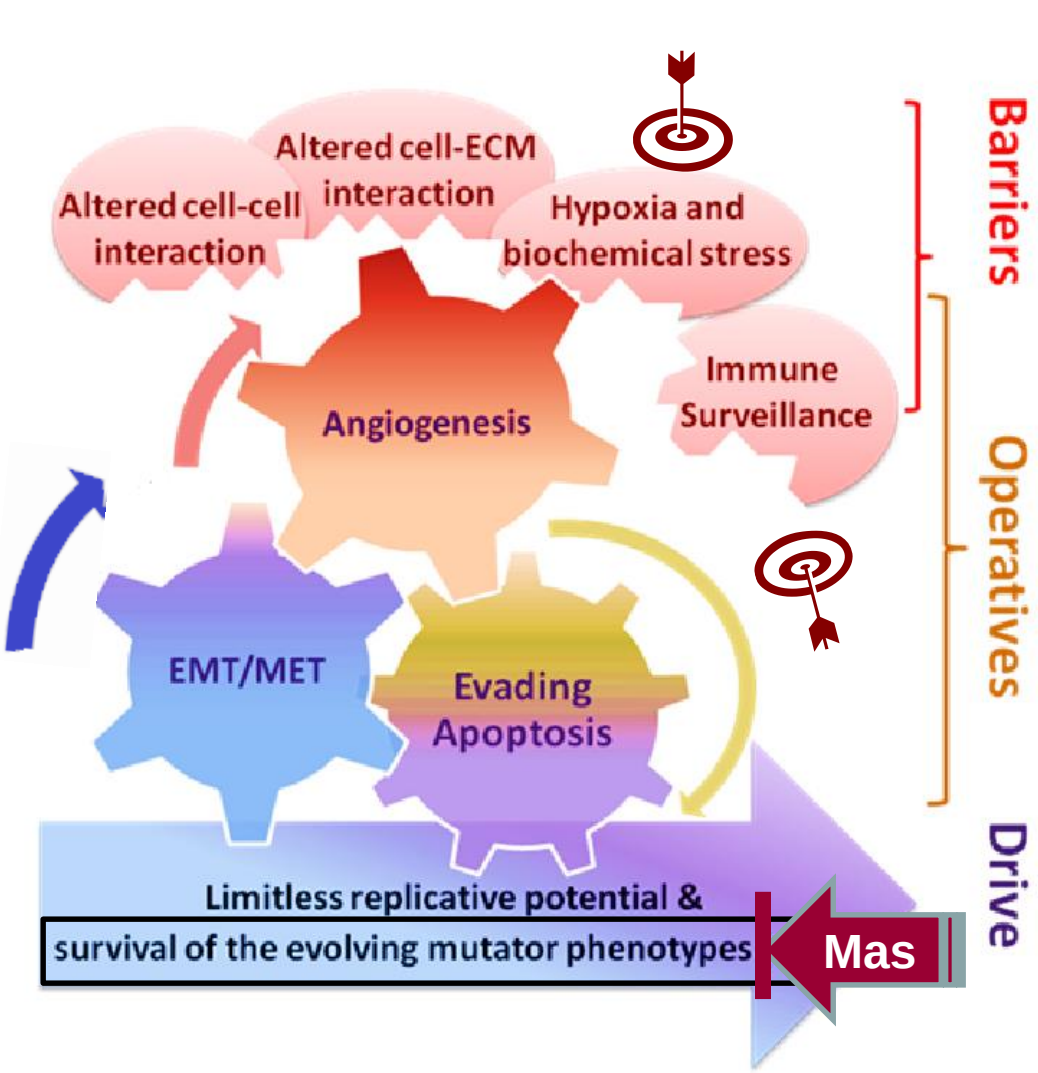
Maspin
Lamin B

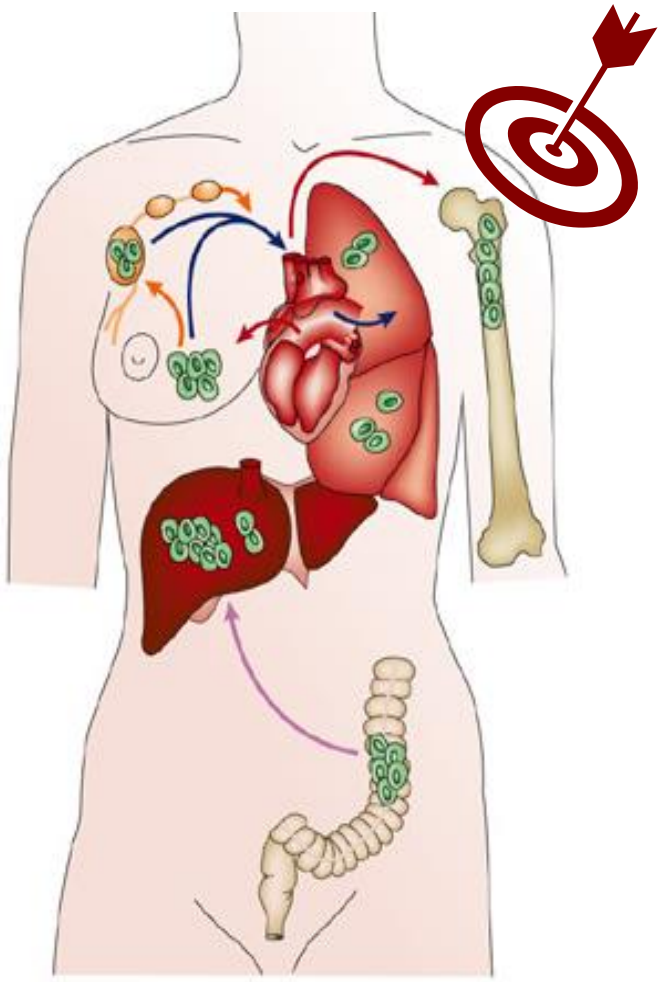


Maspin^{D346E}
Lamin B


WT/HDAC1
D346E/HDAC1
Fos/Jun
ΔFos/Jun
PC3
DU145
Maspin
HDAC1
Merged
WT-GFP/ HDAC1-RFP
D346E-GFP/ HDAC1-RFP

Strategizing Targeted Therapies for Metastasis





THANK YOU!