

Tech Session 1: Cancer

FOTIOS MPEKRIS

CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science

MECHANOTHERAPEUTICS OPTIMIZE THE EFFICACY OF NANO-IMMUNOTHERAPY IN PRECLINICAL BREAST TUMOR MODELS



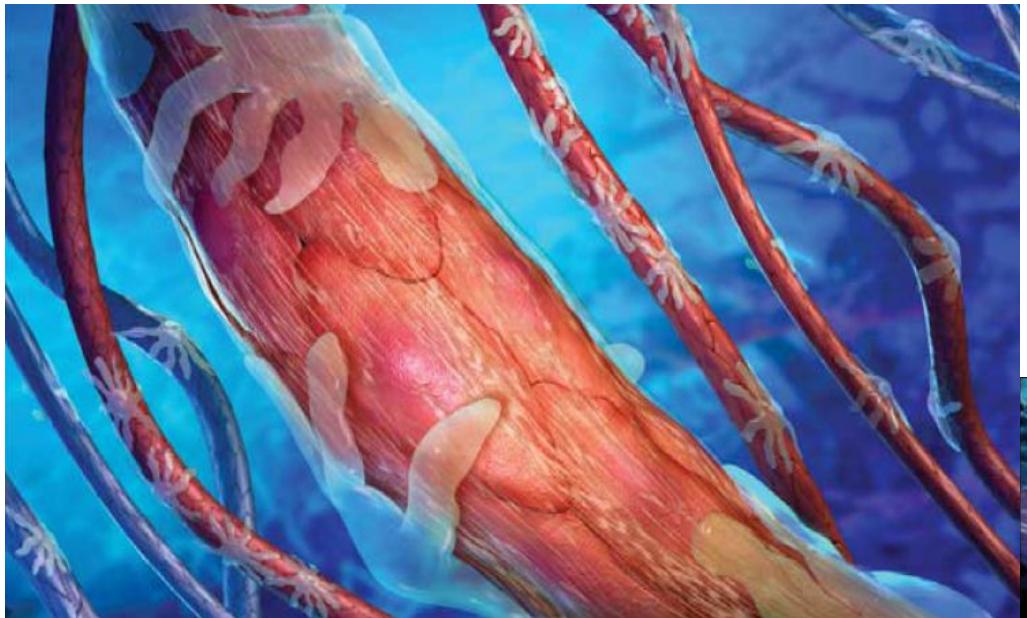
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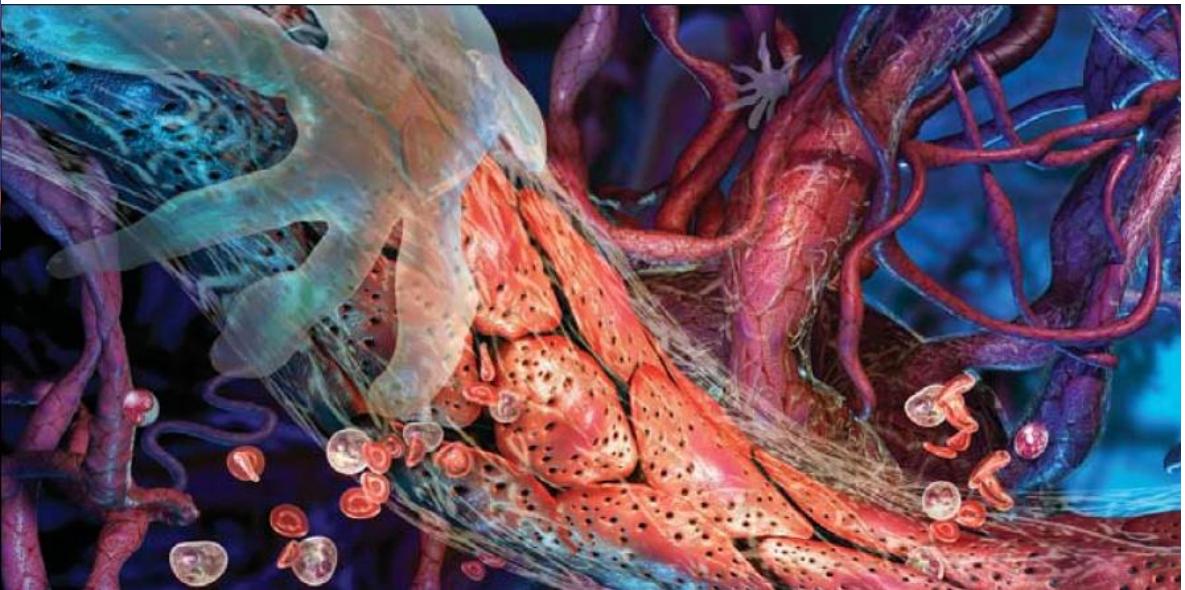


Leakiness of Tumor Vessels



Tumor vessels
(pore size: 10 nm – 2 μ m)

Normal vessels
(pore size: 7-12 nm)



Jain, R. K., *Scientific American*, (2008)



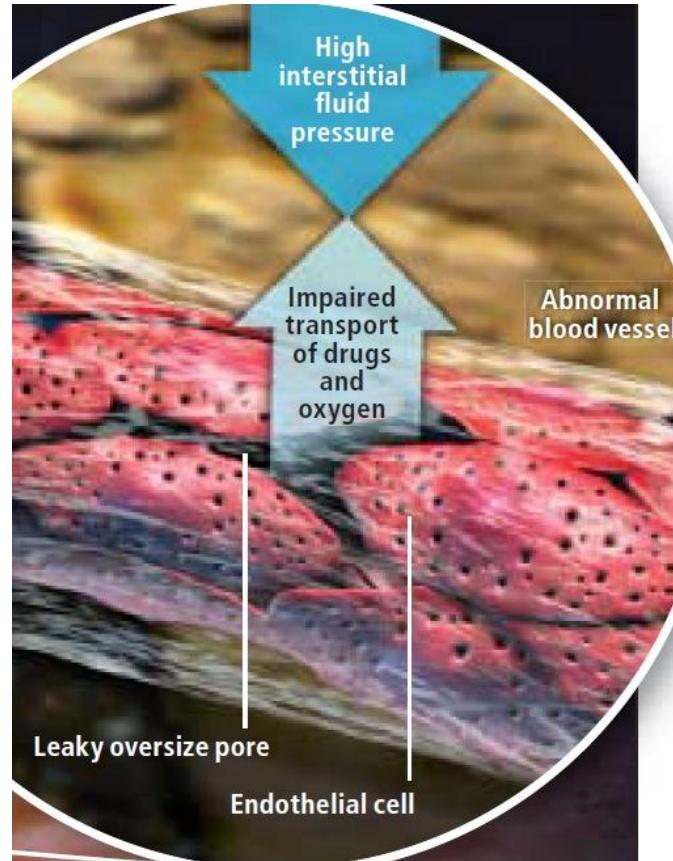
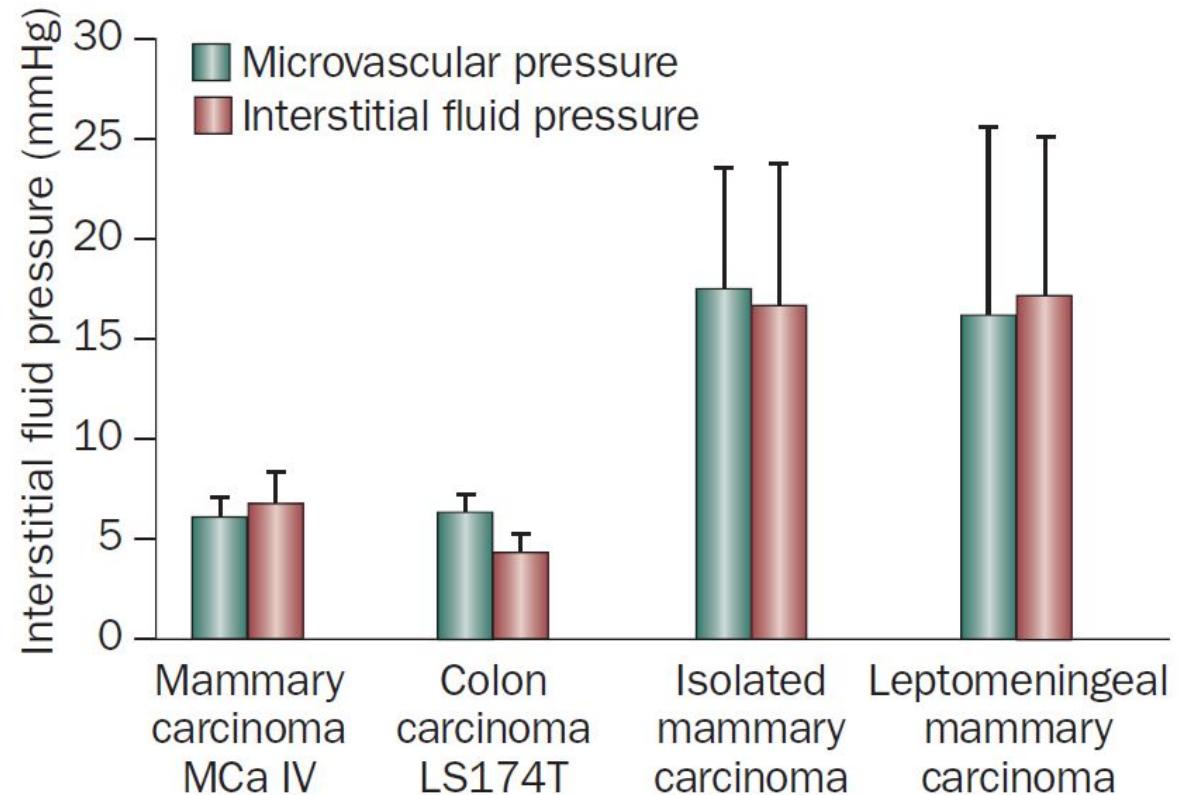
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Fluid phase stresses



Boucher Y. et. al., Cancer Res., (1990)



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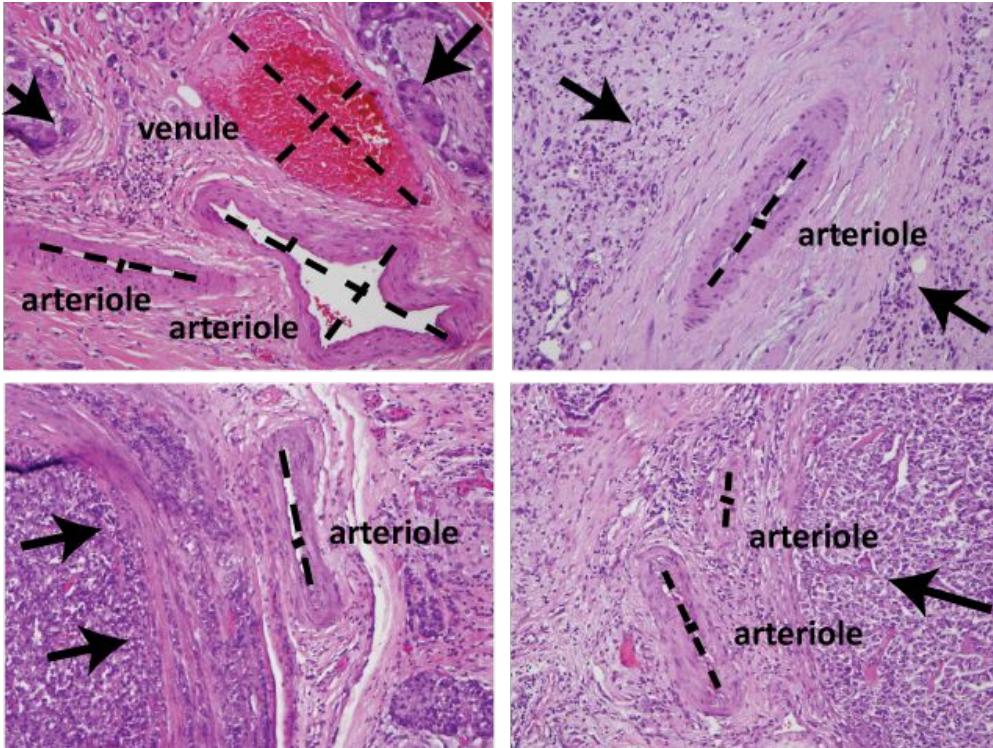
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Compression of blood vessels

Tumor stiffening ↑ Solid stress ↑ → Vessel compression



Stylianopoulos T. et al, PNAS, (2012)

Stylianopoulos T et al., Cancer Research, (2013)



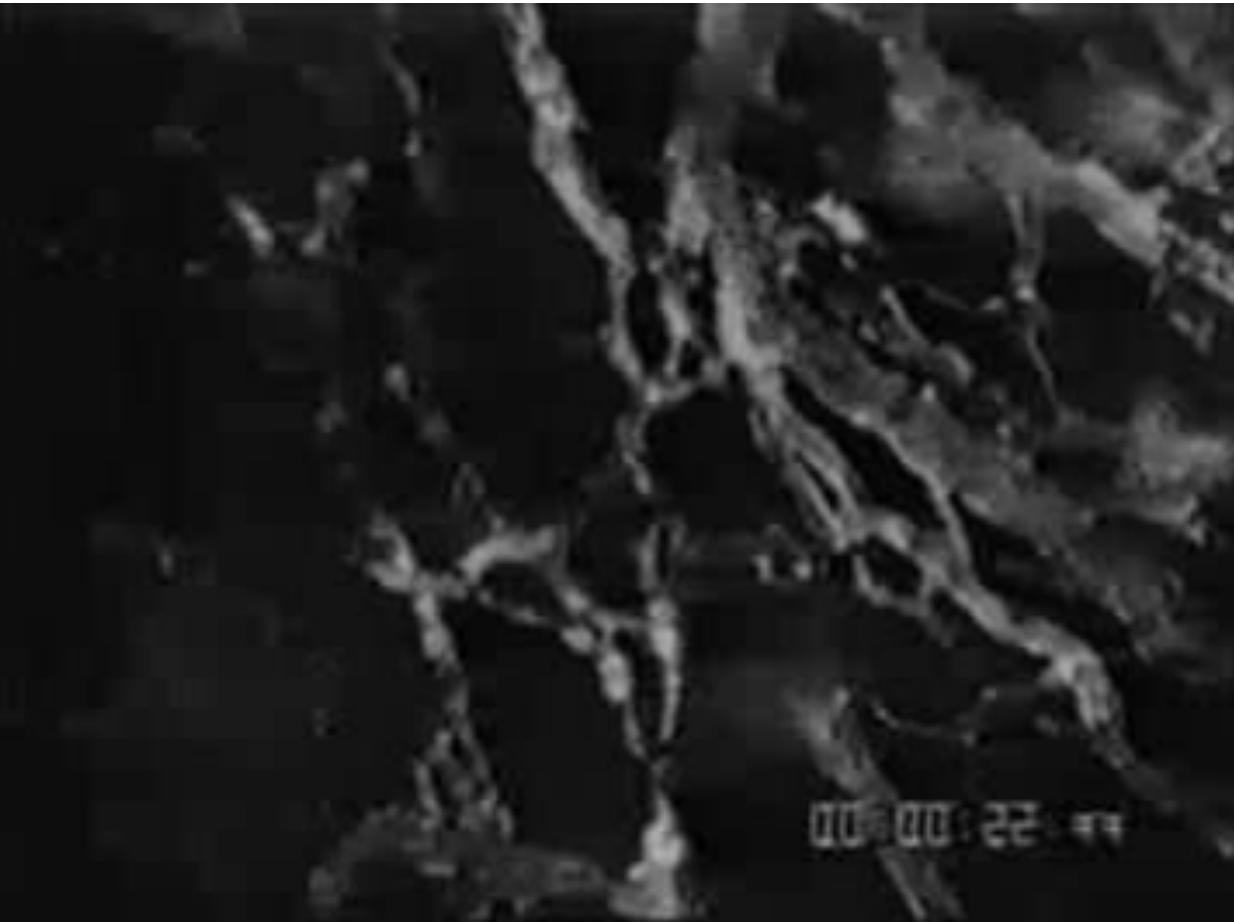
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Heterogeneous Perfusion



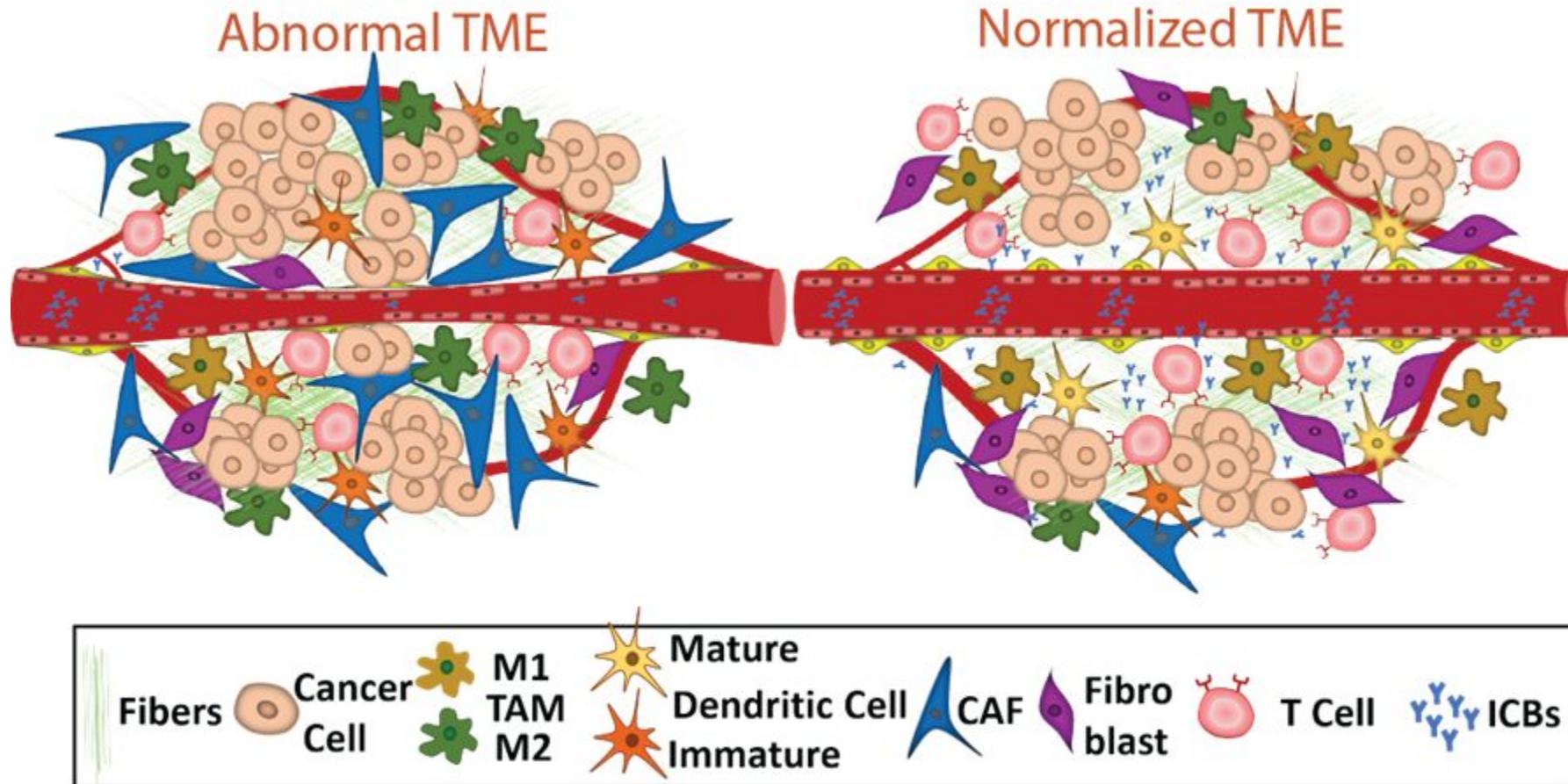
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Re-Engineering Cancer



Stylianopoulos T. et al., Nature Reviews Clinical Oncology (2020)



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Repurpose Tranilast in metastatic murine breast cancer



- Tranilast (Rizaben, Kissei Pharmaceuticals)
- Approved in Japan and S. Korea as an anti-fibrotic and anti-allergic drug.



- Doxil nanomedicine (~100nm)

(P. Papageorgis et al., Scientific Reports, 2017,
Panagi M. et al., Theranostics, 2020,
Mpekris F. et al., Advanced Science 2021)

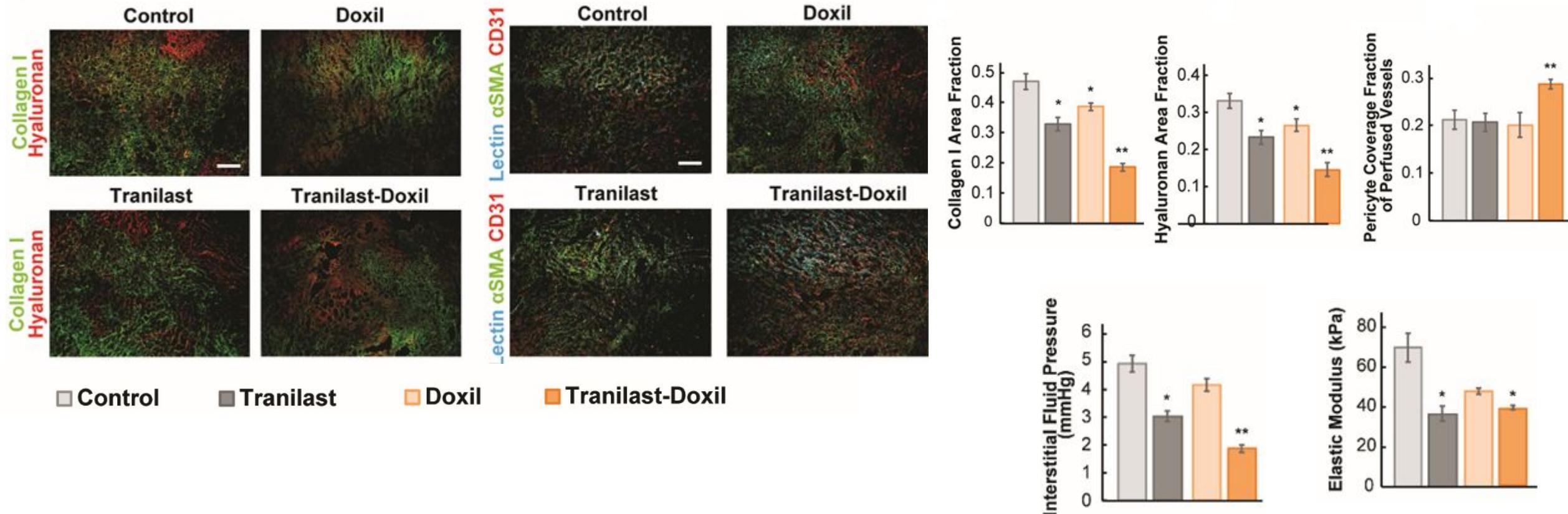


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Nanomedicine enhances tranilast-mediated normalization effects in the primary tumors



Panagi M. et al., Theranostics (2020)
Mpekris F. et al., Advanced Science (2021)

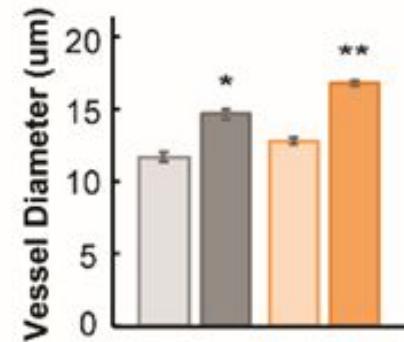
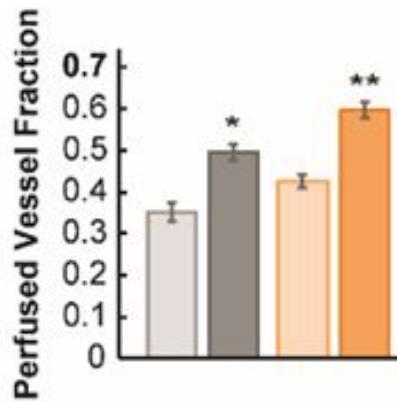
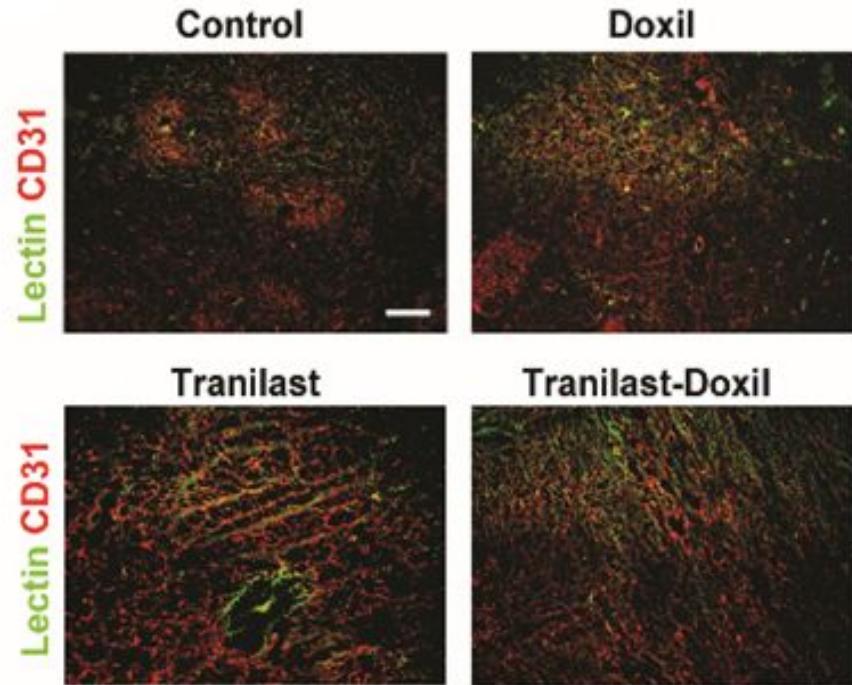
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Nanomedicine combined with tranilast improve perfusion and oxygenation in the primary tumors



Panagi M. et al., Theranostics (2020)
Mpekris F. et al., Advanced Science (2021)

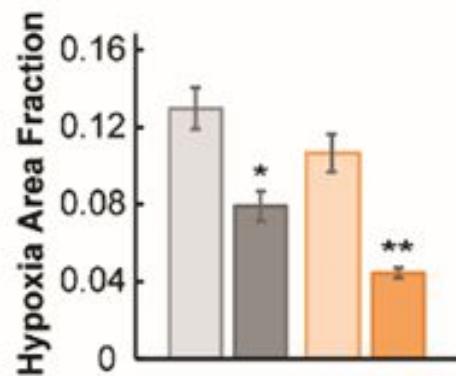
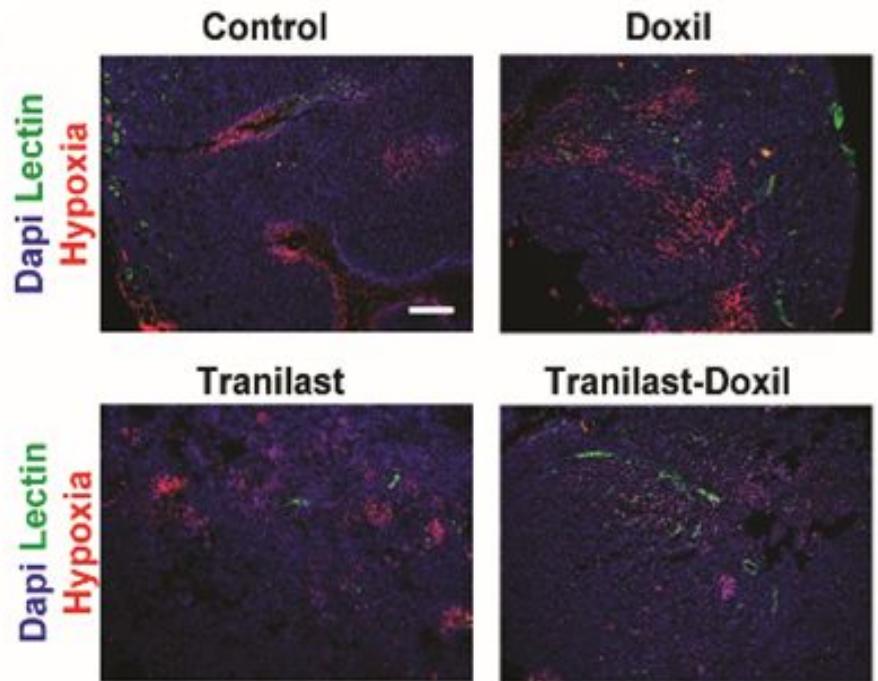


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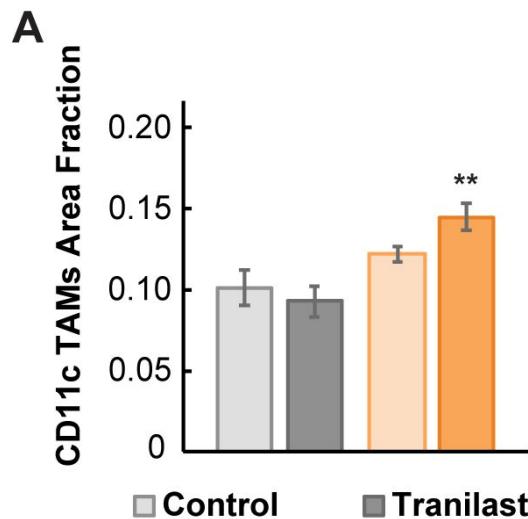
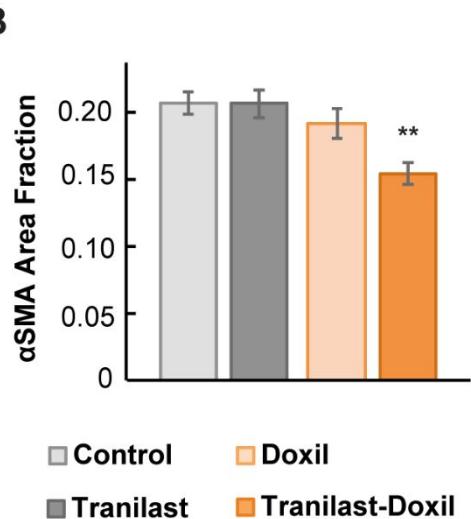
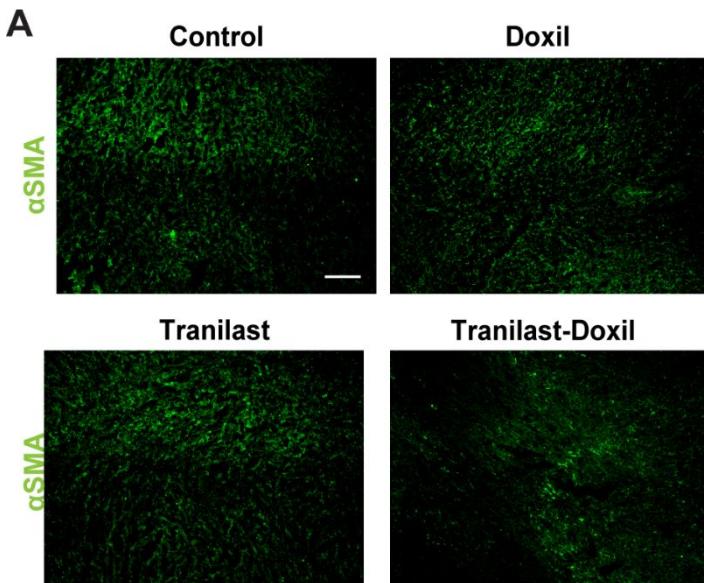
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Nanomedicine combined with tranilast decreased CAFs and skewed TAMs polarization



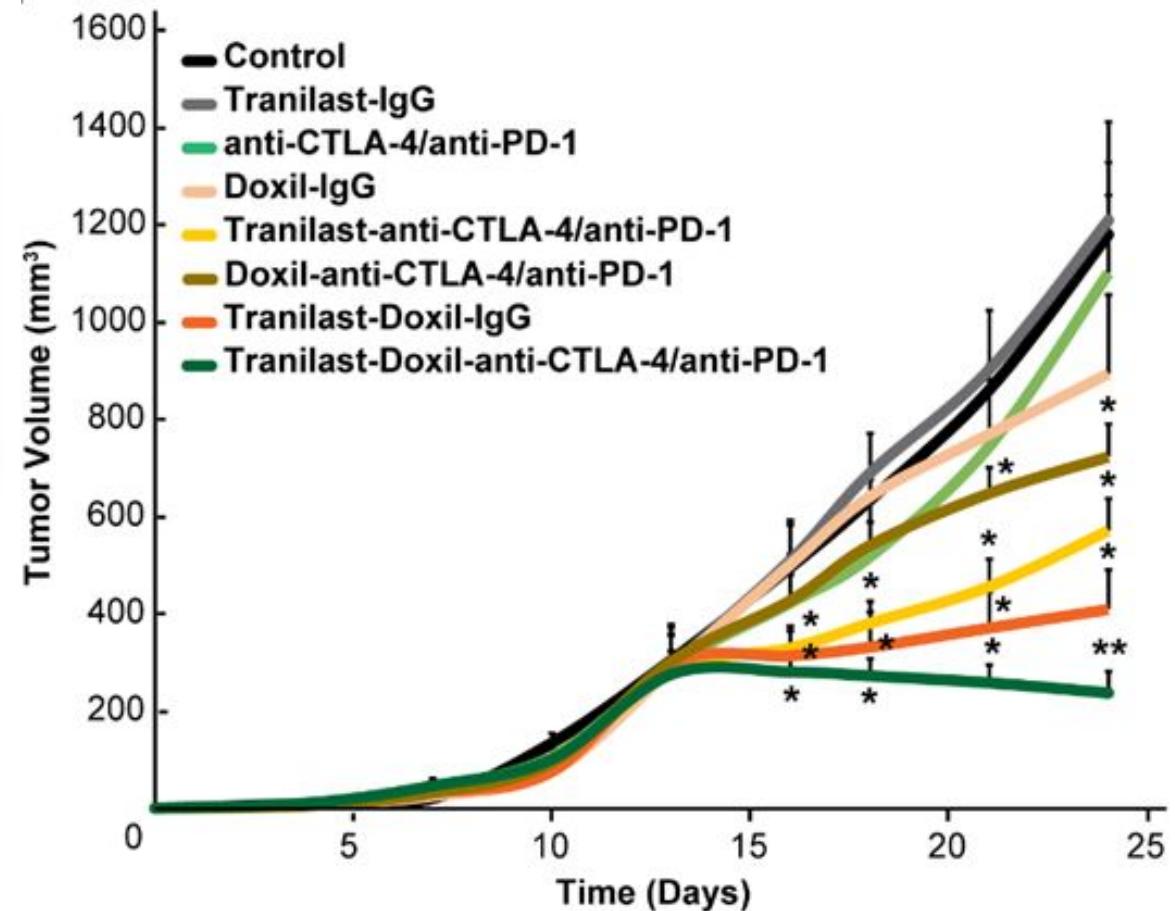
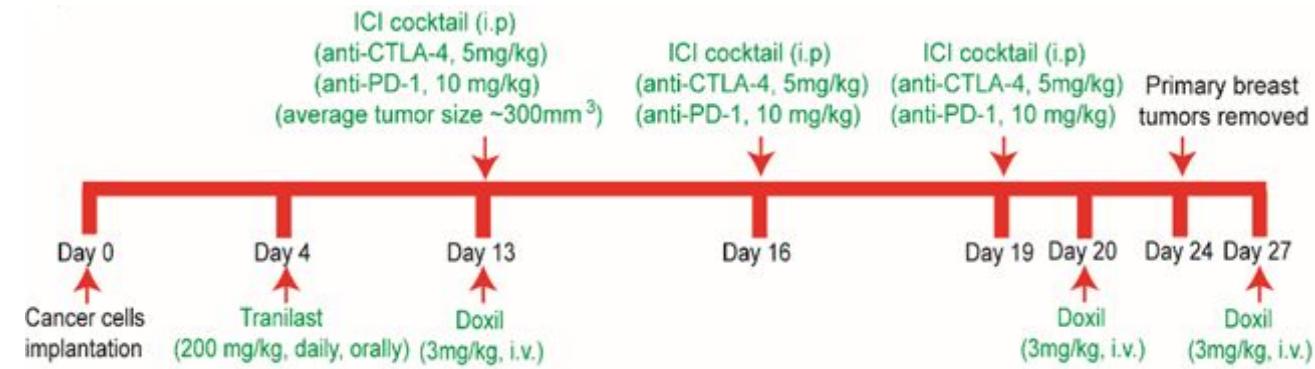
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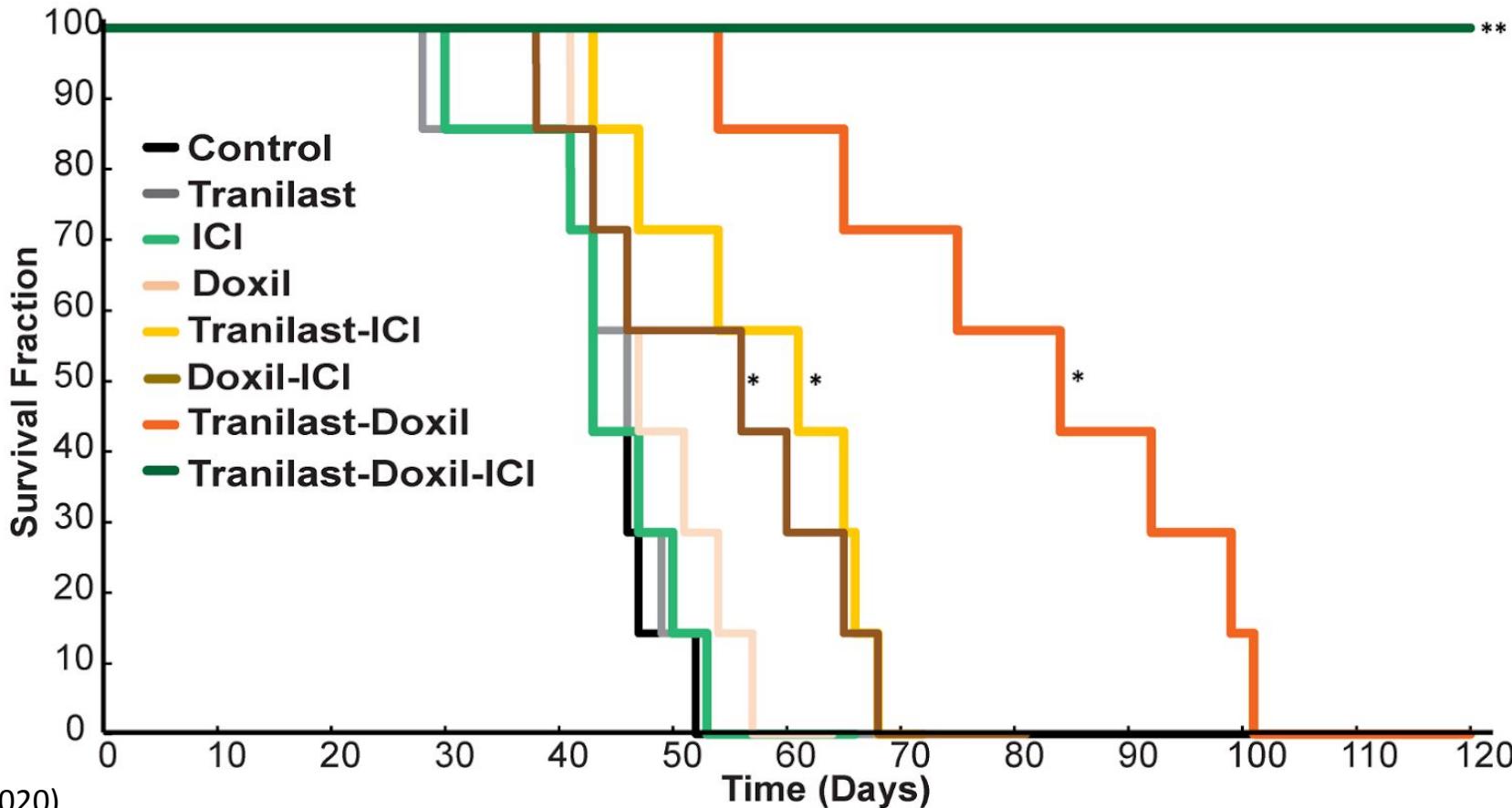
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Enhanced tumor normalization by Doxil and Tranilast improves efficacy of immunotherapy



Panagi M. et al., Theranostics (2020)
Mpekris F. et al., Advanced Science (2021)

Tranilast normalization increases the efficacy of nano-immunotherapy leading to cure



Panagi M. et al., Theranostics (2020)

Mpekris F. et al., Advanced Science (2021)

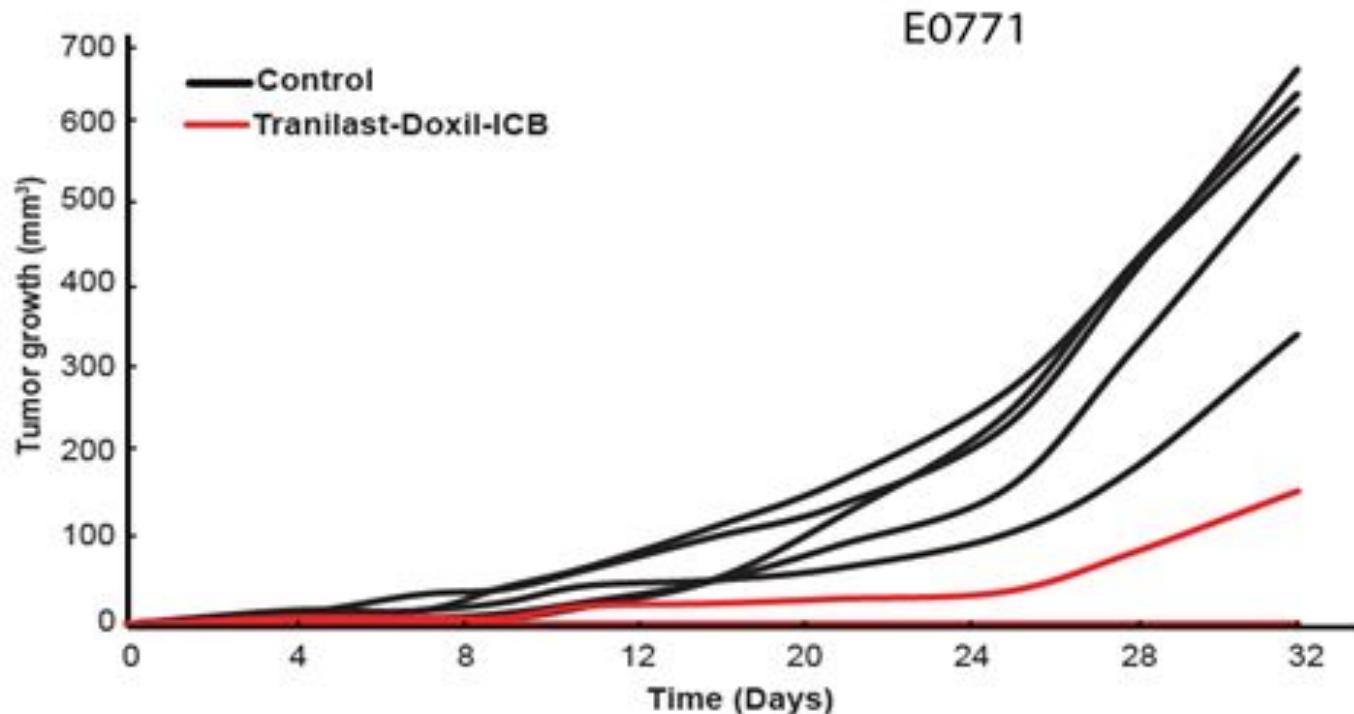


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Immunological memory to cancer-associated antigens

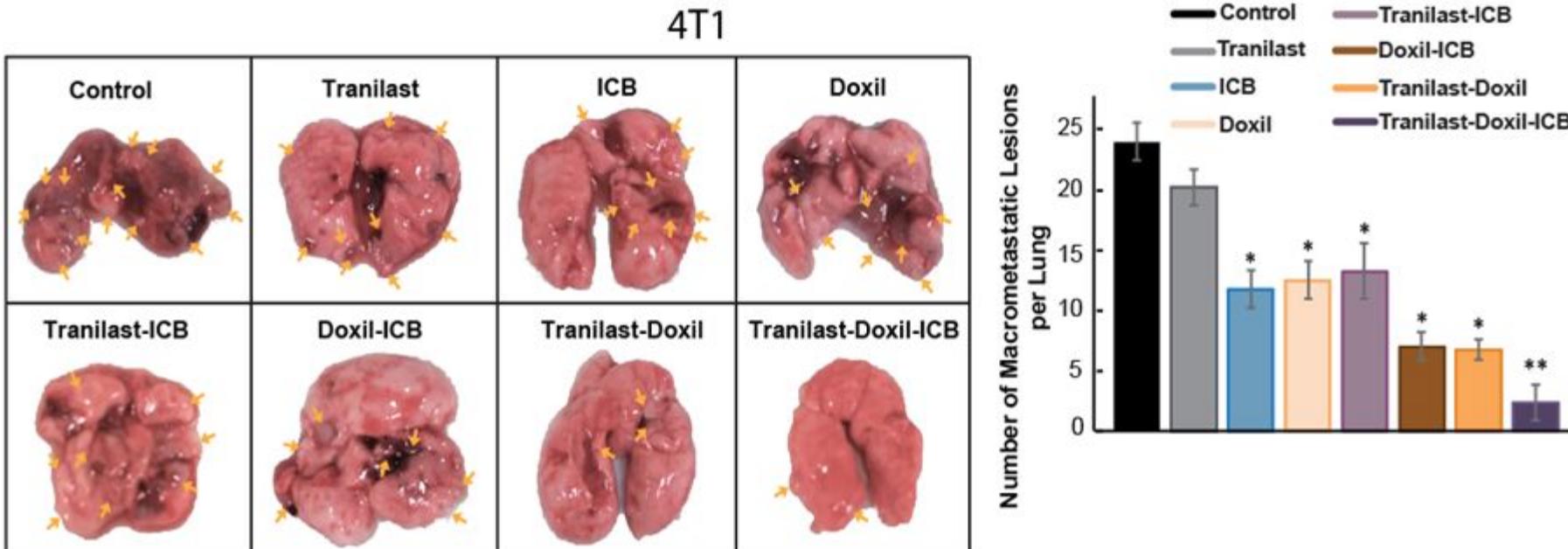


- Cells were implanted again in a different mammary fat pad of the mice.
- Tumor grew in all control mice,
- Only one grew in the treated mice
- Combination of tranilast with Doxil and ICB treatment provides evidence of immunological memory of the mice to E0771 cancer cells.

Panagi M. et al., Theranostics (2020)
Mpekris F. et al., Advanced Science (2021)



Tranilast normalization increases the efficacy of nano-immunotherapy in metastases



Panagi M. et al., Theranostics (2020)
Mpekris F. et al., Advanced Science (2021)



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Acknowledgements



Triantafyllos Stylianopoulos^a
John D. Martin^b
Horacio Cabral^b
Kazunori Kataoka^c

^a Cancer Biophysics Laboratory, University of Cyprus

^b Department of Bioengineering, Graduate School of Engineering, University of Tokyo,

^c Innovation Center of NanoMedicine, Kawasaki Institute of Industrial Promotion, Kanagawa, Japan



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