



Synergistic Tumor Microenvironment Modulation Enhances Nano-Immunotherapy and Chemotherapy Across Solid Tumors

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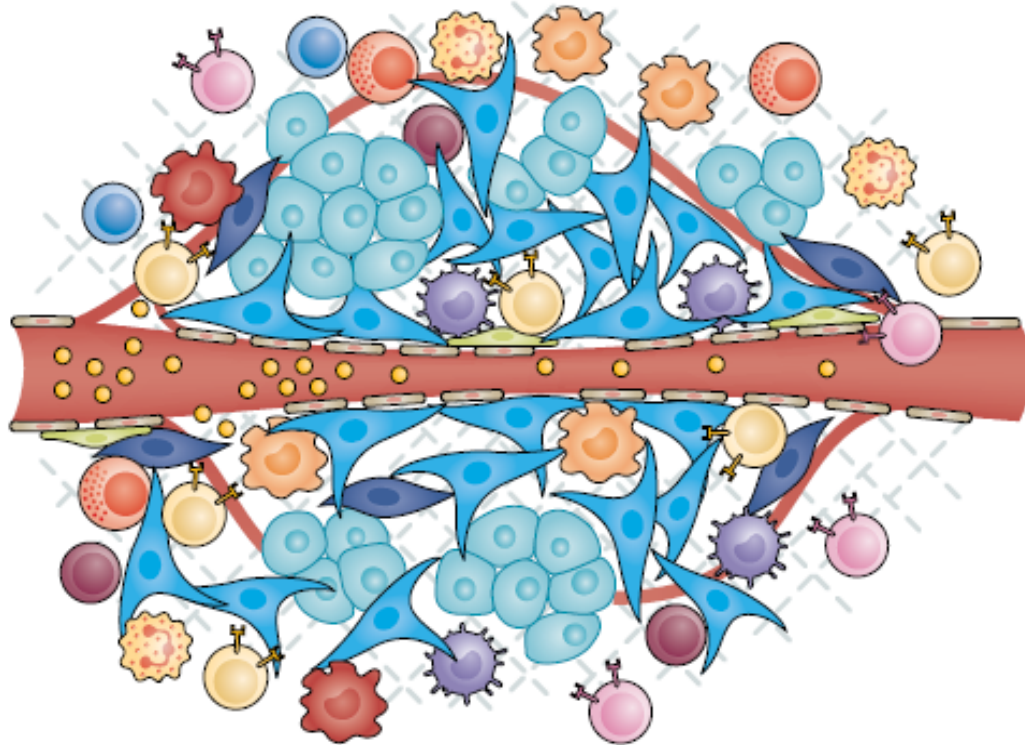


MULTISECTOR
INNOVATION
for ADVANCING
DELIVERY SCIENCE
JULY 6-9, 2026

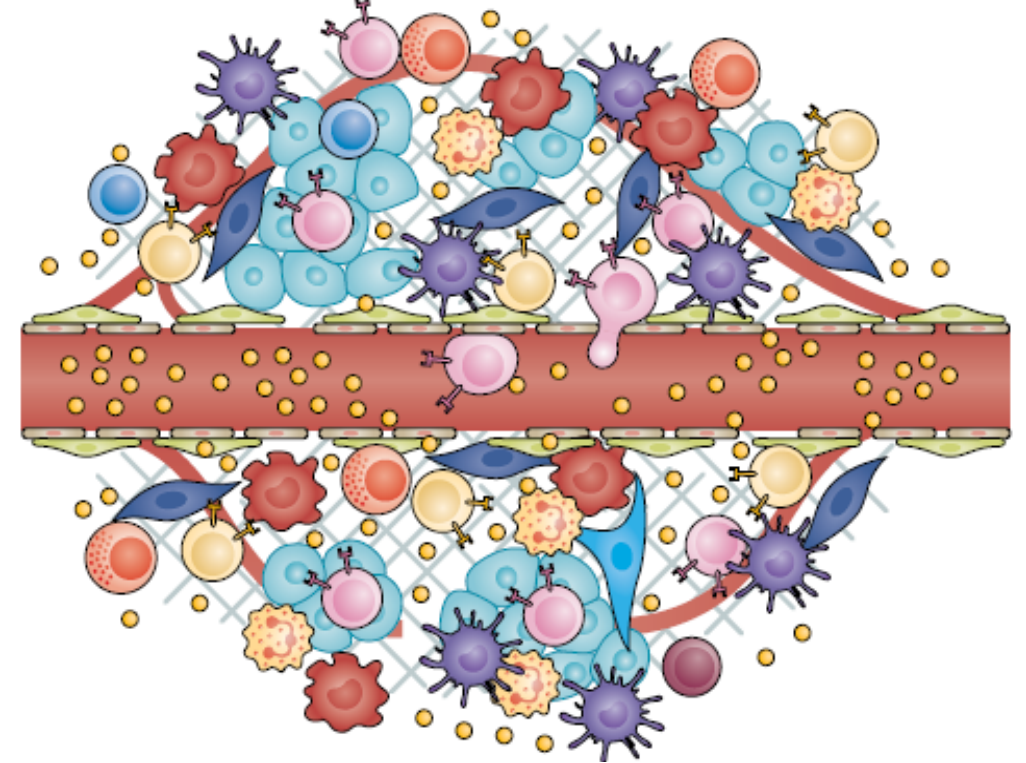


Re-engineering Cancer

The TME compromises delivery



TME normalization increases delivery



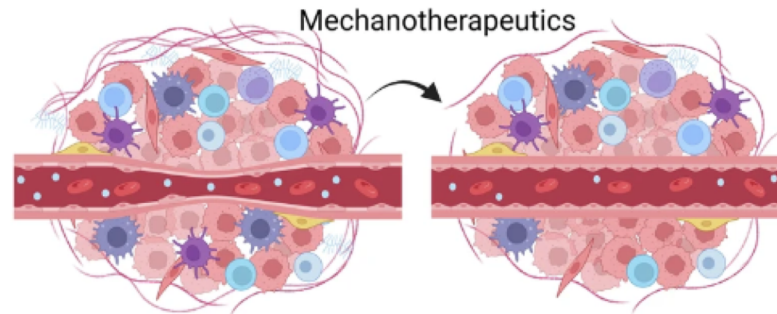
Martin JD, et al, Nature Reviews Clinical Oncology, 2020



The promise of mechanotherapeutics and sonopermeation

Mechanotherapeutics

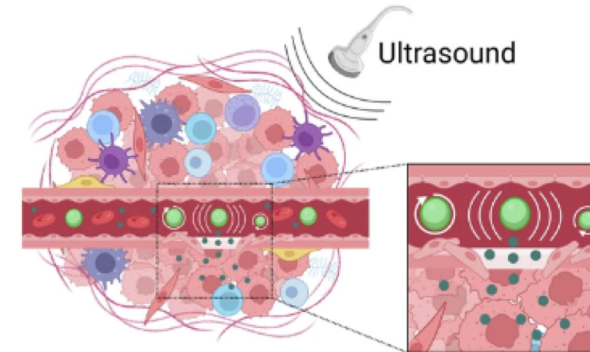
- ✓ Modulate mechanical forces in tumors
- ✗ Can decompress only 40% of the vessels



- ✓ Mechanotherapeutics open vessels for sonopermeation

Sonopermeation

- ✓ Enhance tumor perfusion non-invasively
- ✗ Collapsed vessels cannot deliver microbubbles



- ✓ Sonopermeation further alleviates mechanical forces

Multiplicative Synergistic effects

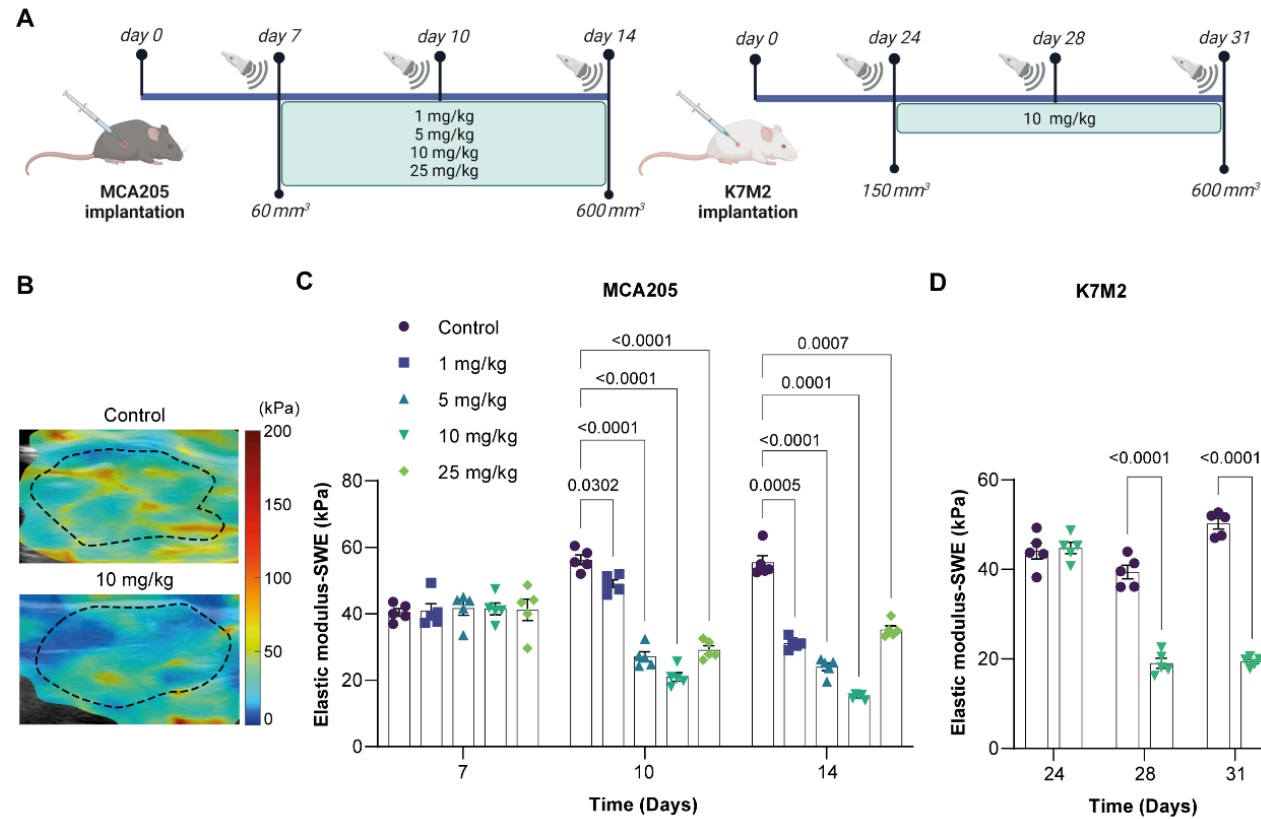
- ECM Components
- Mechanical Forces
- Immunosuppressive Cells
- Cancer cells Proliferation



- Tumor Perfusion
- Drug Delivery
- Immunosupportive Cells
- Treatment Efficacy



Ketotifen decreases mechanical forces



Panagi M. et al, Clinical Cancer Research, 2024



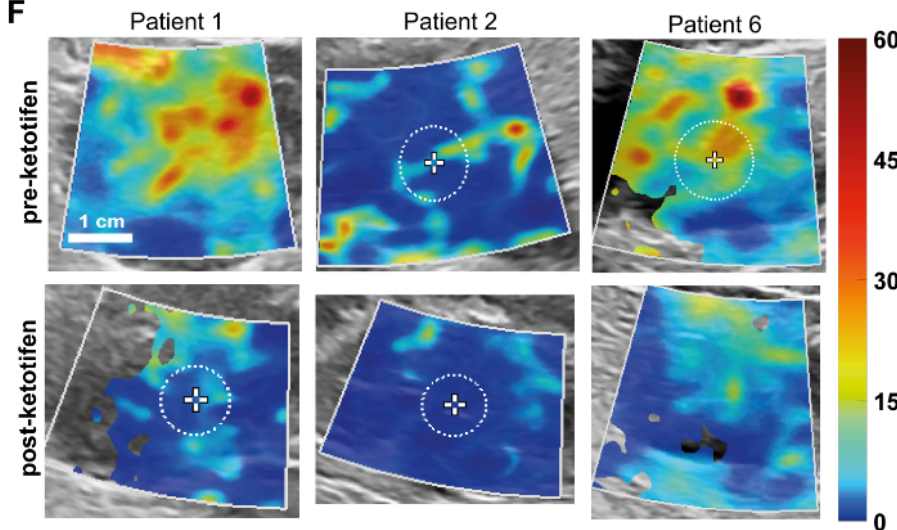
Ketotifen decreases mechanical forces

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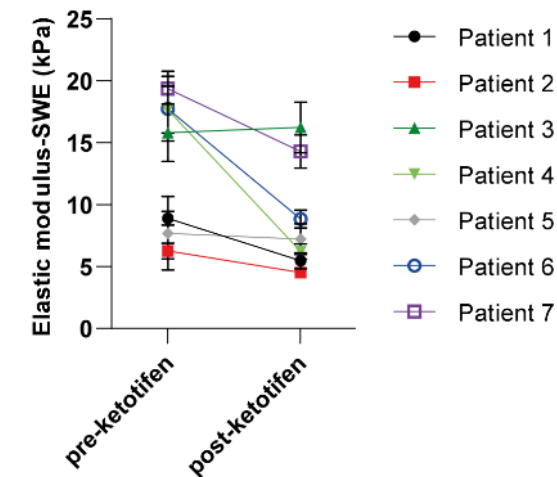
Demographics and clinical characteristics				SWE			
	Diagnosis	Age	Gender	Baseline stiffness (kPa)	Post-ketotifen stiffness (kPa)	Treatment duration (days)	p value ^a
Patient 1	Epithelioid leiomyosarcoma	70	F	8,90	6,70	123	0,026
Patient 2	Myxofibrosarcoma	66	F	6,26	4,50	155	0,048
Patient 3	Atypical lipomatous tumor	62	F	15,80	16,23	8	0,890
Patient 4	Leiomyosarcoma	69	M	17,66	6,21	140	1,5E-04
Patient 5	Pleomorphic leiomyosarcoma	47	F	7,68	7,21	8	0,881
Patient 6	Synovial sarcoma	79	M	17,74	8,835	55	0,006
Patient 7	Desmoid tumor	31	F	19,36	14,29	7	0,020

^a P values are from non-parametric T-test, significant p values are in bold

F



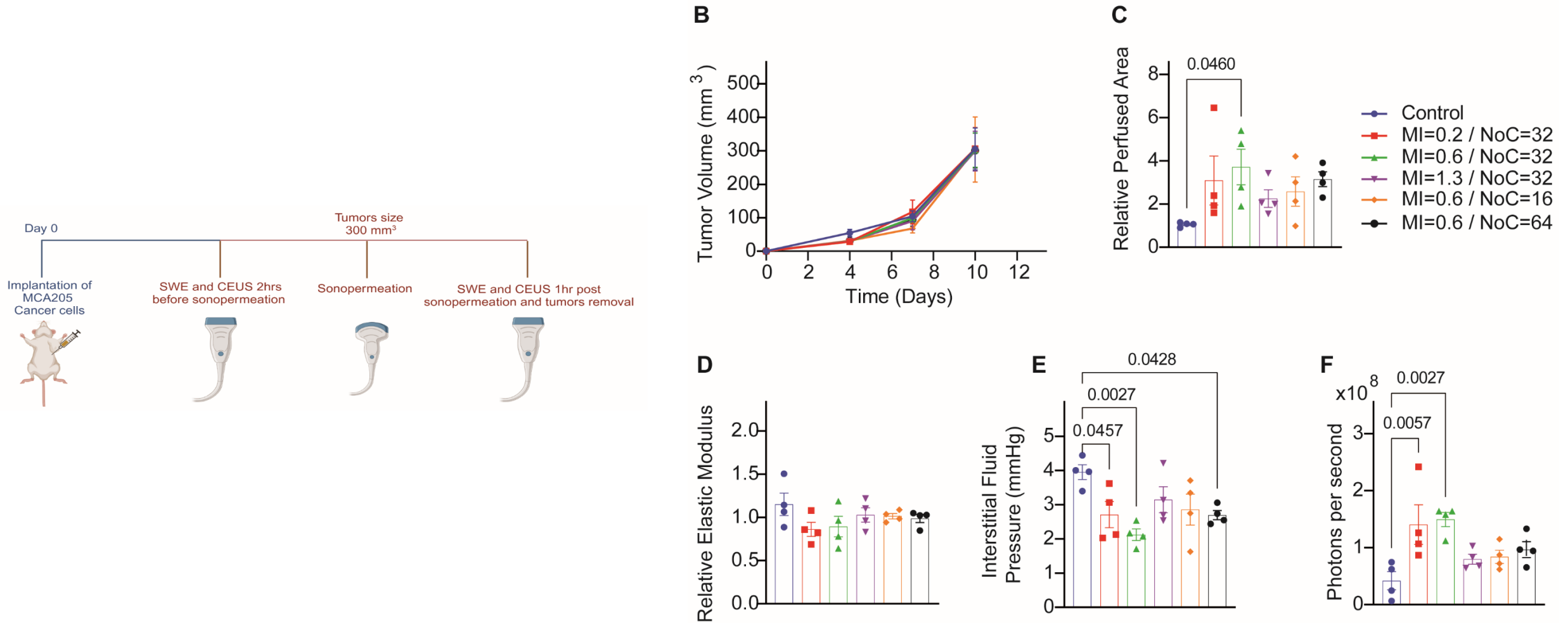
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Panagi M. et al, Clinical Cancer Research, 2024



Sonopermeation improves tumor perfusion



Mpekris F. et al, Neoplasia, 2024



Combined treatment improves the efficacy of nano-immunotherapy and chemotherapy



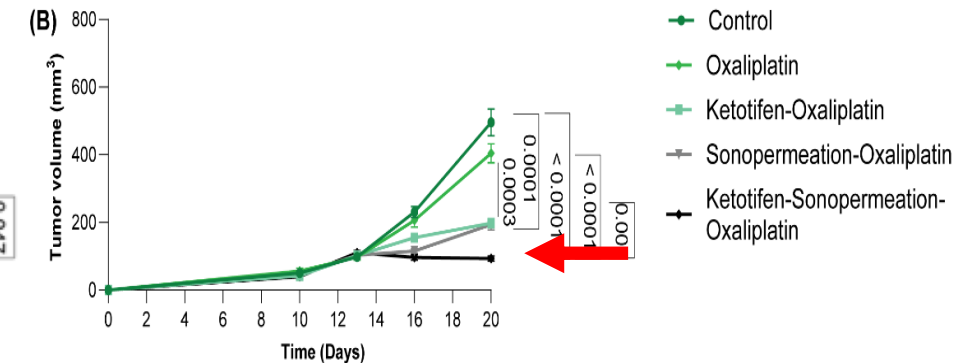
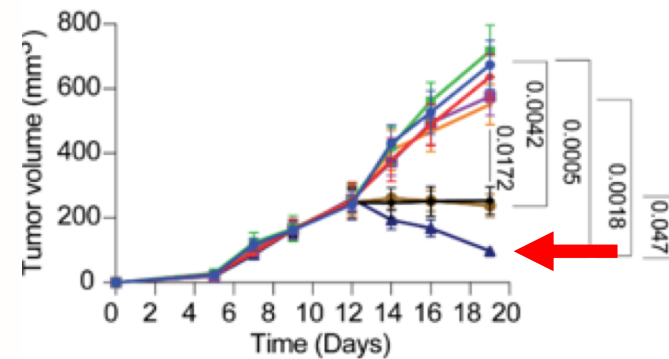
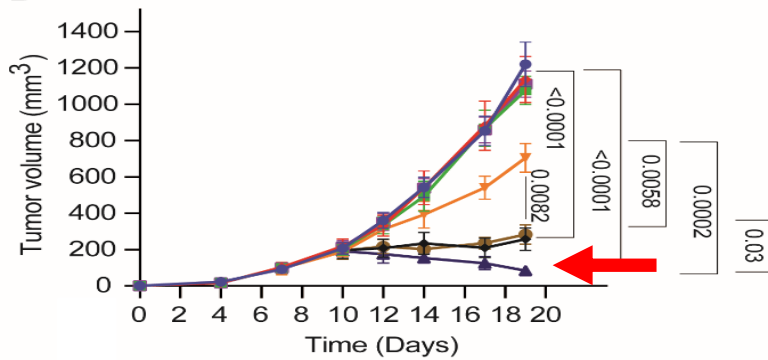
Control

Ketotifen-Sonopermeation-Doxil-ICIs

Sarcomas

Breast

Pancreatic

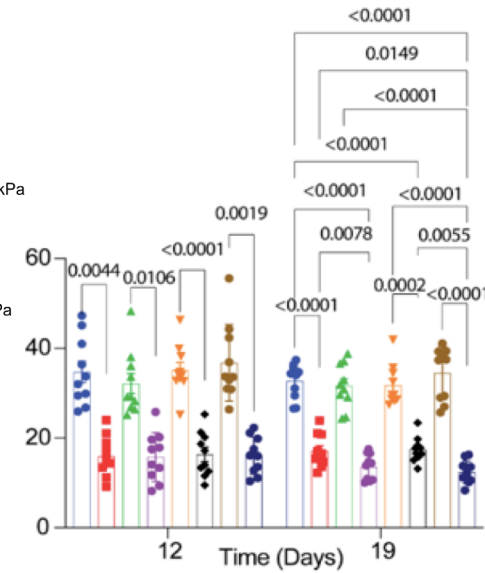
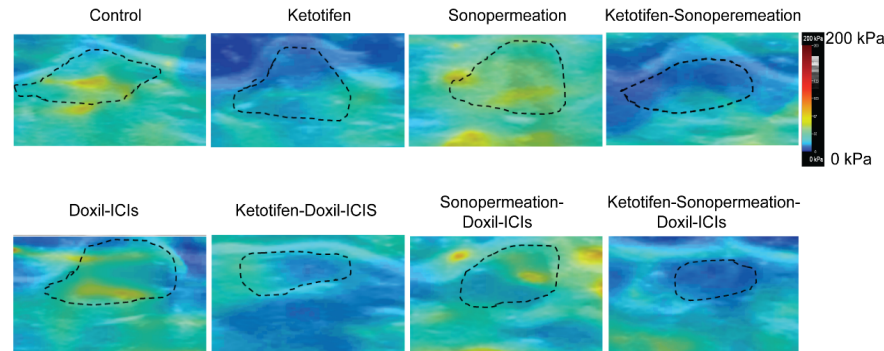


- Control
- Ketotifen
- Sonopermeation
- Ketotifen-Sonopermeation
- Doxil-ICIs
- Ketotifen-Doxil-ICIs
- Sonopermeation-Doxil-ICIs
- Ketotifen-Sonopermeation-Doxil-ICIs

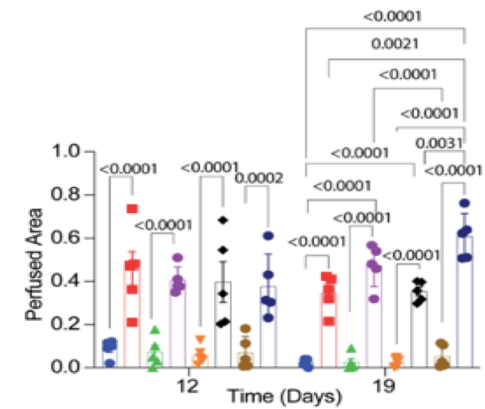
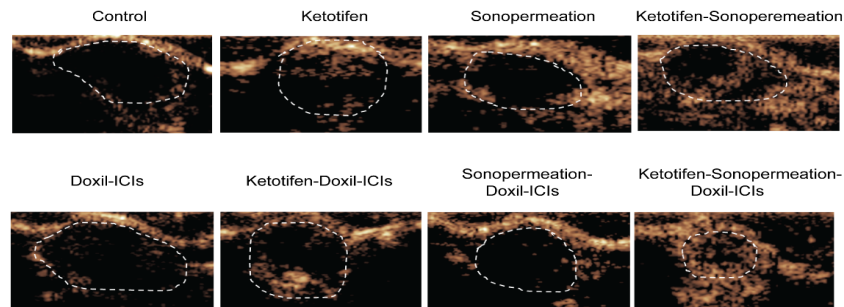


Combined treatment effectively normalizes the TME

US Elastography- Stiffness

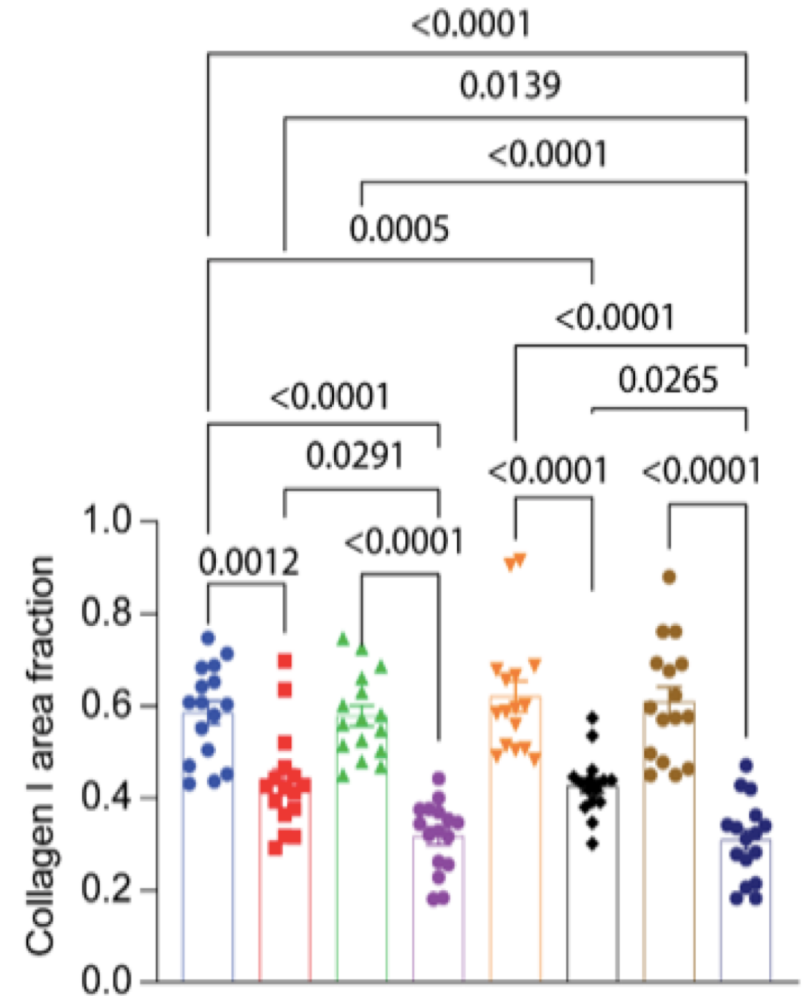
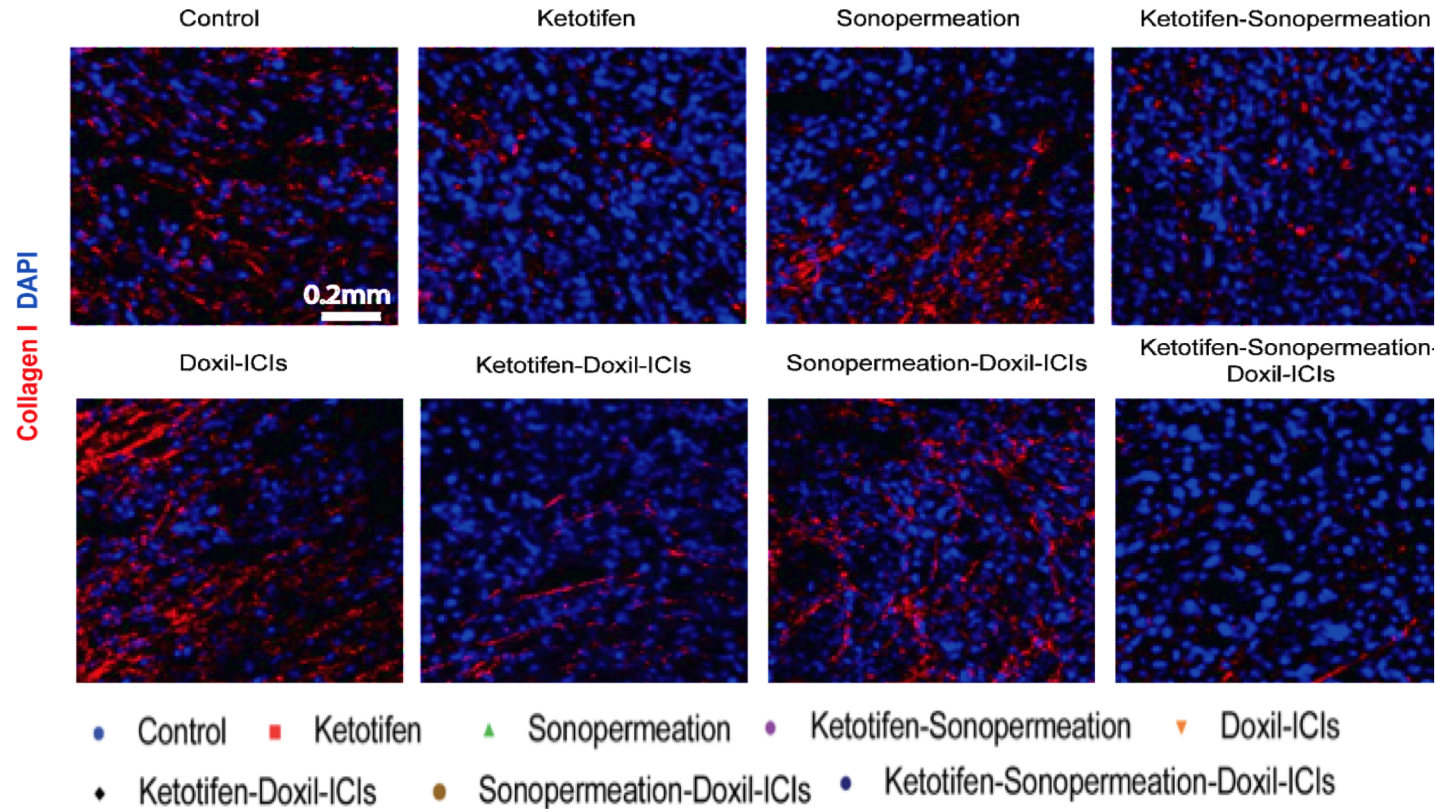


Contrast Enhanced US- Perfusion



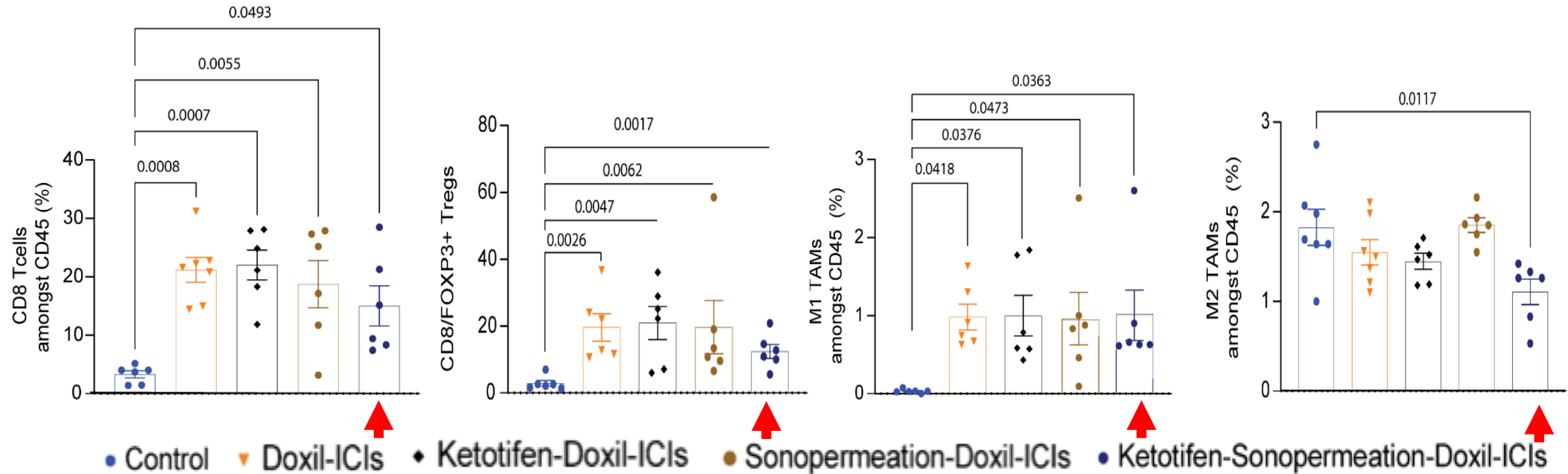
Combined treatment effectively normalizes the TME

Histology



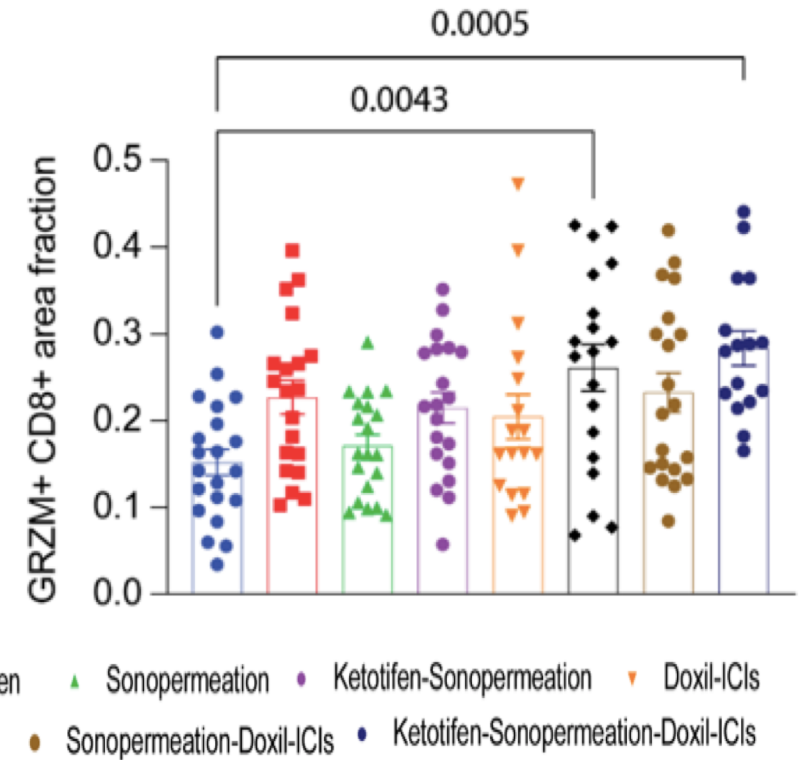
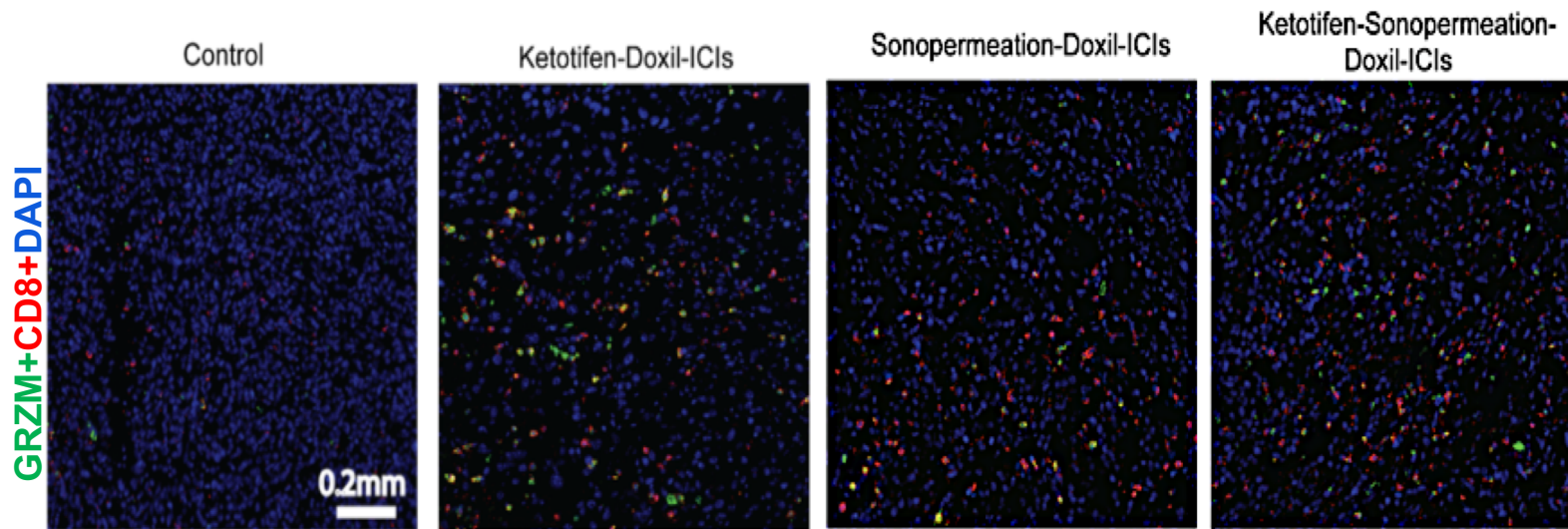
Ketotifen, sonopermeation and nano-immunotherapy/chemotherapy promotes immune cells infiltration and immunostimulation

Flow Cytometry



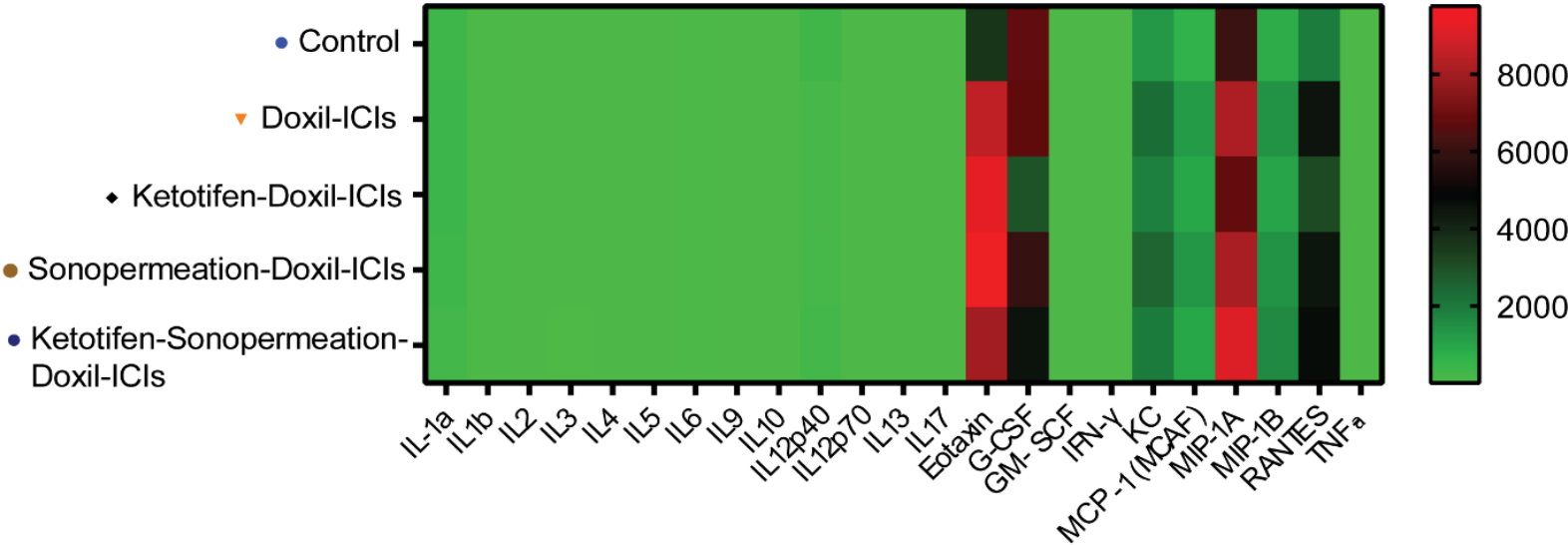
Ketotifen, sonopermeation and nano-immunotherapy/chemotherapy promotes immune cells infiltration and immunostimulation

Histology- activated CD8⁺ cells expression

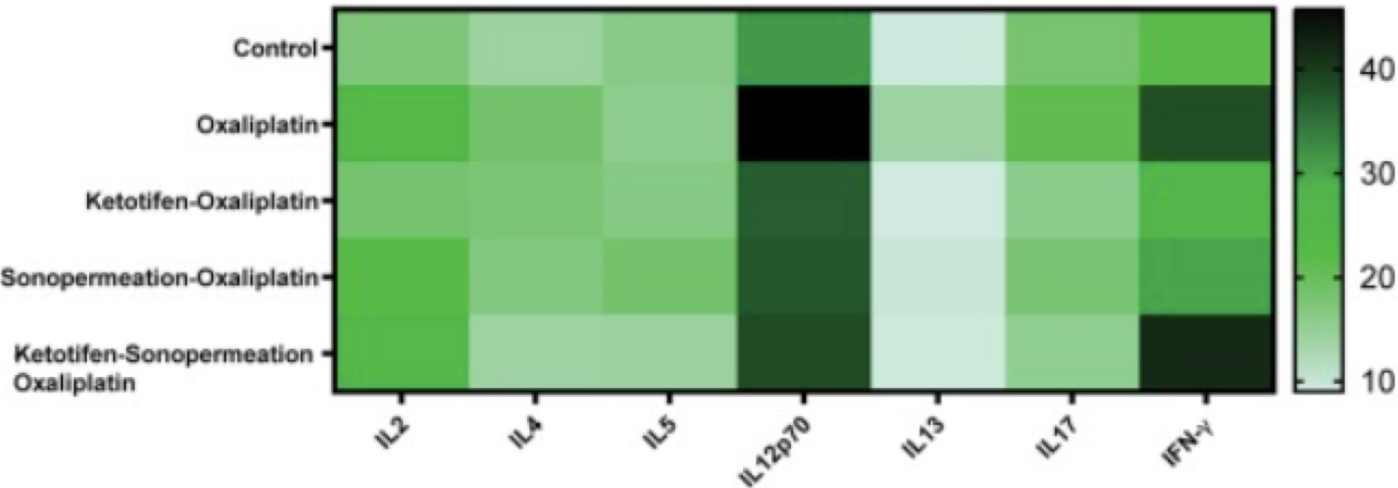


Effect of combination therapy in cytokines

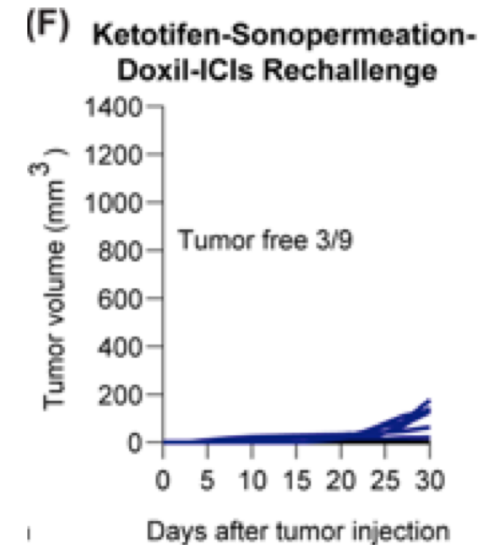
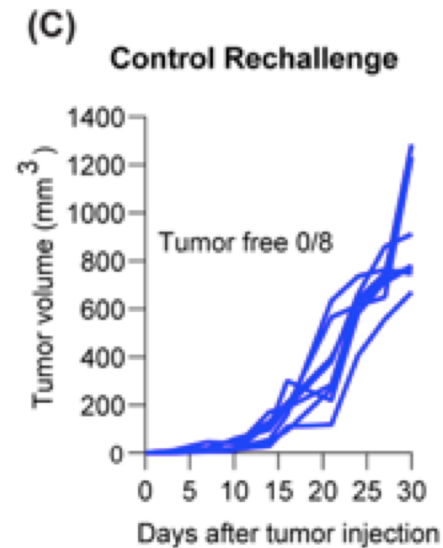
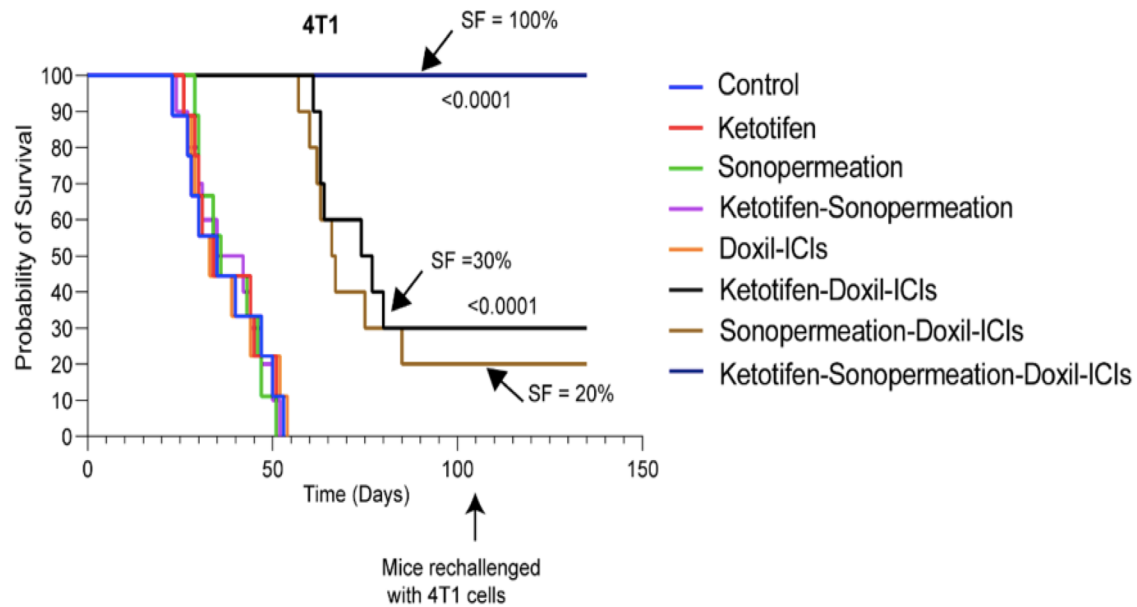
BREAST



PANCREATIC

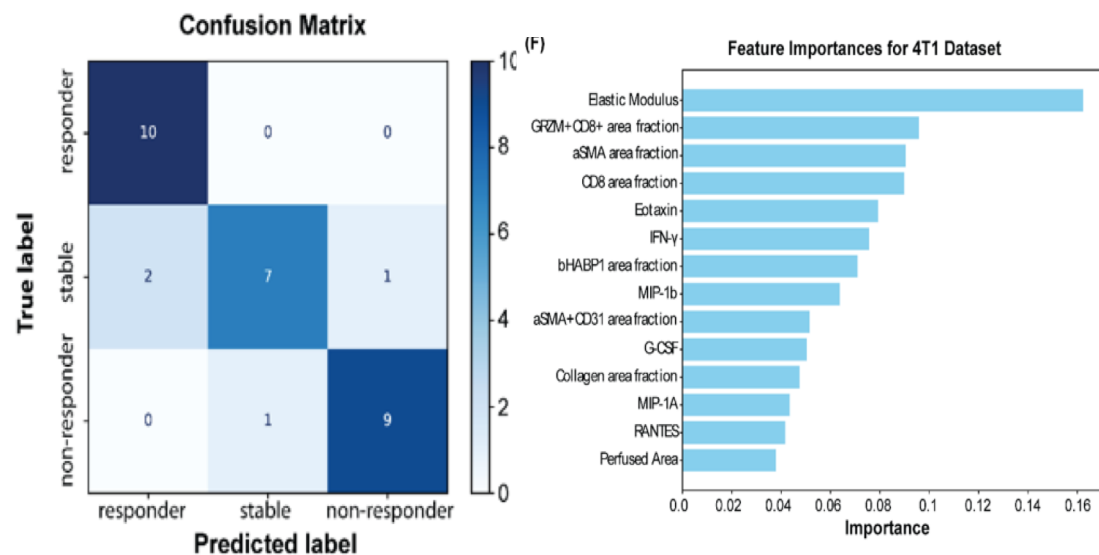


Combination of ketotifen and sonopermeation markedly enhances nano-immunotherapy efficacy in breast tumors

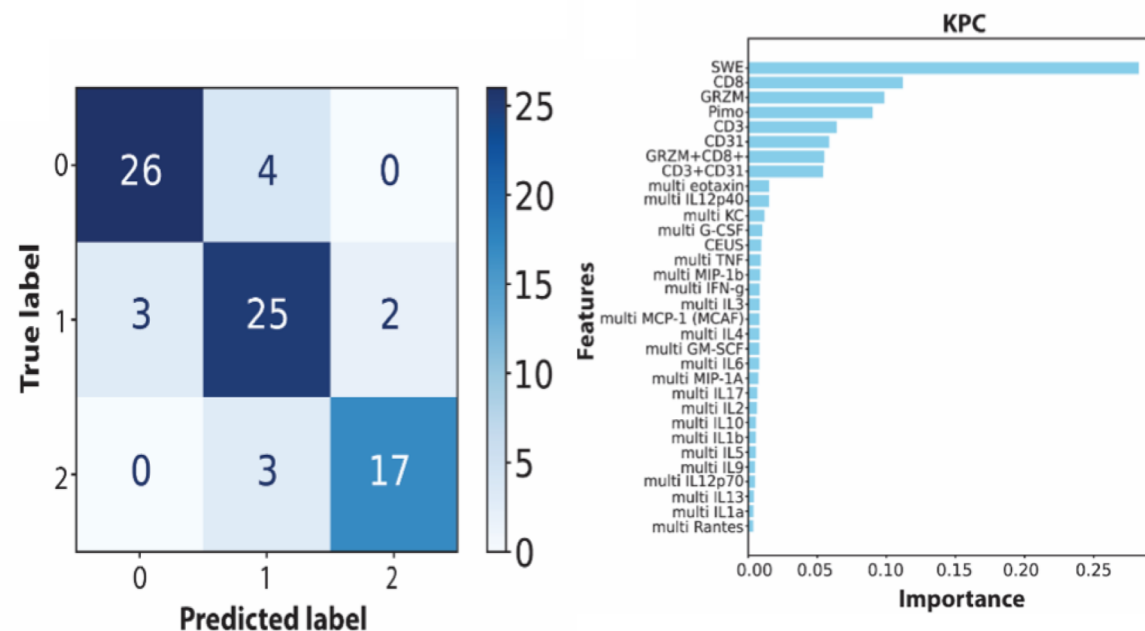


Machine learning analysis of collected data reveals biomarkers predictive of response

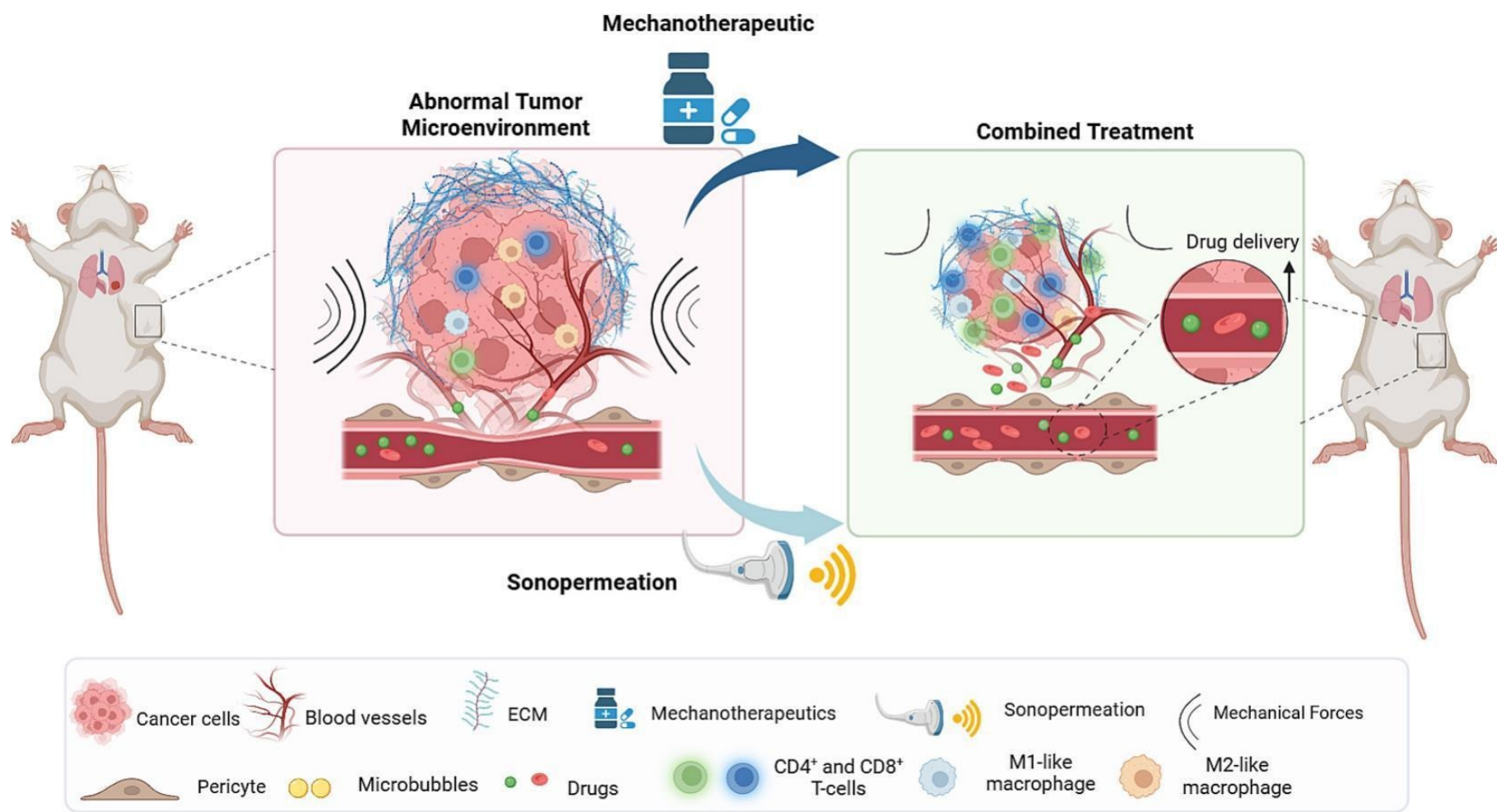
BREAST



PANCREATIC



Key Take-Home Message: Re-engineering the Tumor Microenvironment to Overcome Therapy Resistance



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