Micro-milled high-throughput force sensor array for in situ mechanical testing of tumors-on-a-chip

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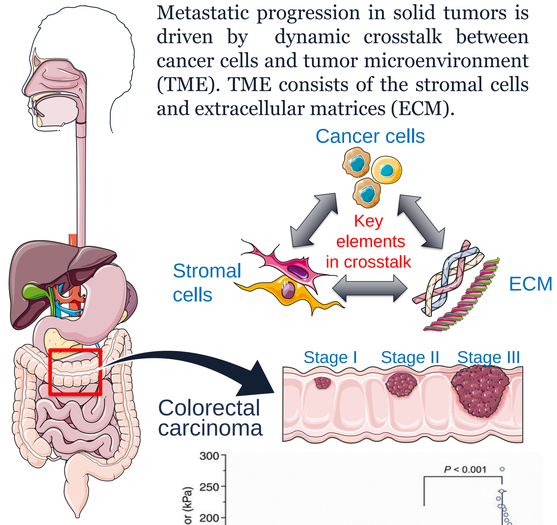
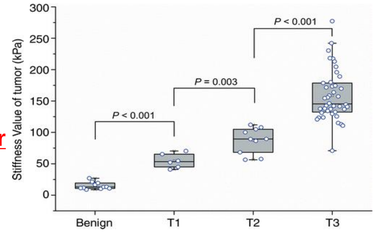
BACKGROUND



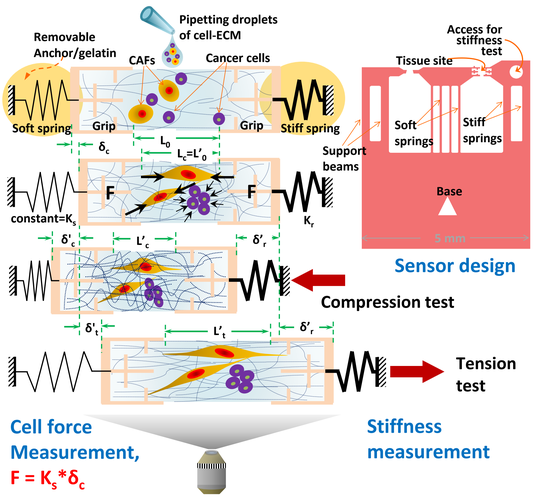
Metastatic progression in solid tumors is driven by dynamic crosstalk between cancer cells and tumor microenvironment (TME). TME consists of the stromal cells and extracellular matrices (ECM).

Solid tumors become **stiffer** with time and growth [1].

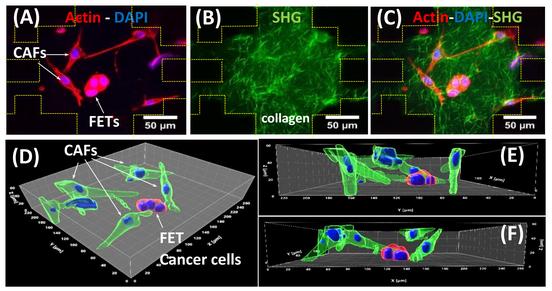


NOVEL BIOPHYSICAL SENSOR [2]

Design principles

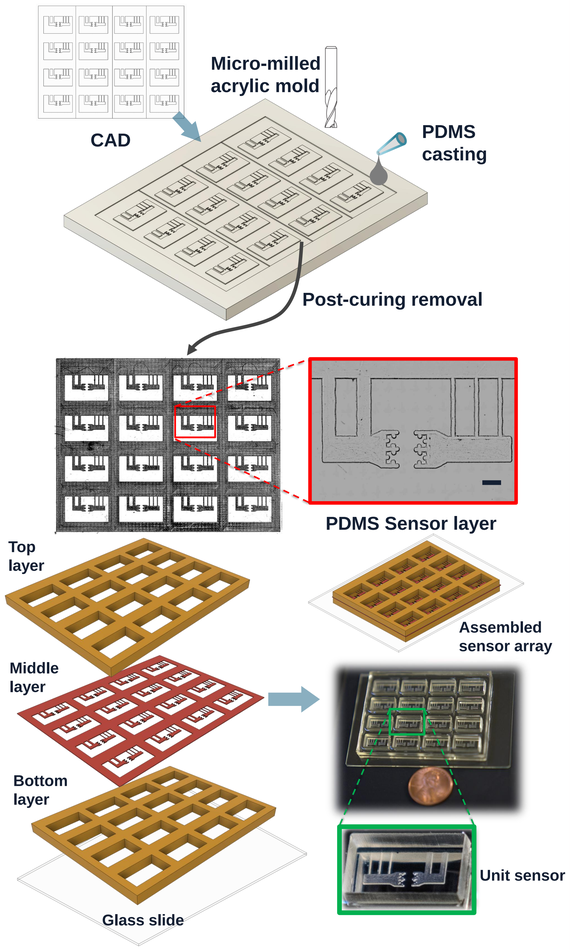


3D TUMOR-ON-A-CHIP



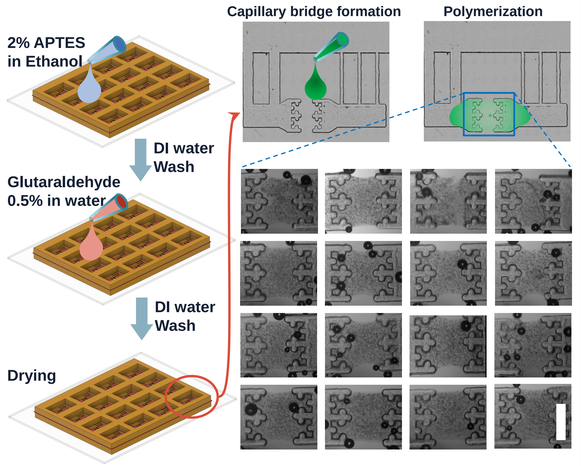
HIGH-THROUGHPUT ARRAY

Fabrication



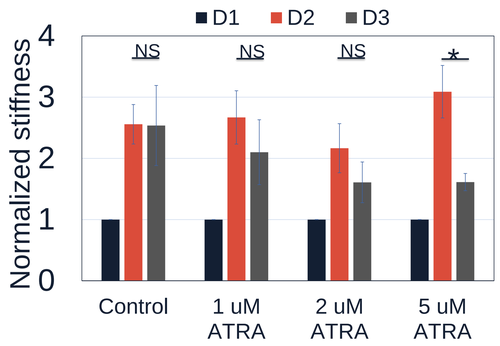
HIGH-THROUGHPUT ARRAY

Tissue formation

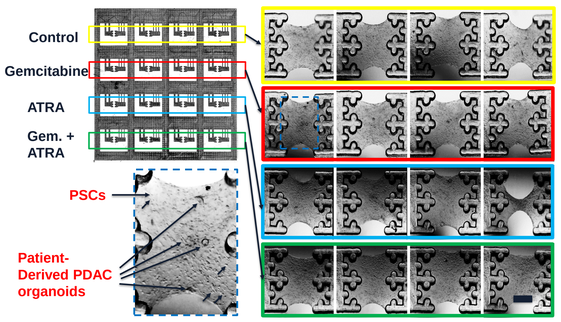


RESULTS

CRC CAFs with ATRA

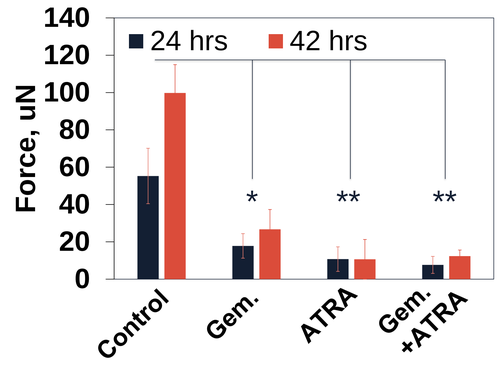


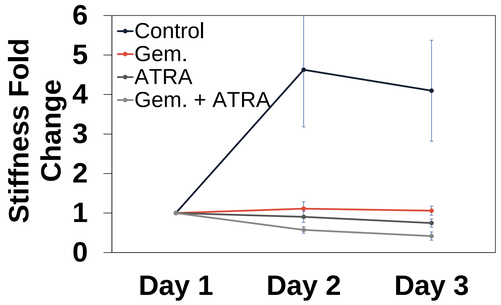
Patient Derived PDAC models



RESULTS

ATRA reduces matrix stiffening





CONCLUSIONS

- A 3D tumor models constructed on a novel biophysical sensor provide total cell force and stiffness change from matrix remodeling.
- Fabricated using cost-effective and scalable micro-milling technique, the sensor array allows for multiple specimens within a single dish enhancing experimental throughput.
- ATRA (all-trans retinoic acid) is effective in alleviating matrix stiffening by the CAFs.
- Combination of Gemcitabine and ATRA inhibits force and matrix stiffening in patient-derive PDAC models.

REFERENCES

1. Chen, L. da et al.. Radiology 285, 279–292, 2017
2. Emon, B. et al. Science Advances, 7(15), 2021

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