

# Mechanism of Mechanical Microenvironmental Control of Cancer Metastasis

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## Objectives

- To understand the effect of coupled mechanical cues and geometric cues on the onset of 2D in vitro colon cancer metastasis.
- Investigate the role of dimensionality (2D vs 3D) and biophysical environment on colon cancer cell behavior using a 3D cell culture model.

## Research Highlights

- Recently, our group has shown that human colon carcinoma (HCT-8) cells show metastasis like phenotype (MLP) in vitro when cultured on appropriate intermediate mechanical stiffness (21-47 kPa) substrates, but not on very soft (1 kPa) and very stiff substrates (3.6 GPa) [1], Fig. 1a].
- Development of a novel micropatterning technique to spatially confine cell adhesion molecules (e.g Fibronectin, Laminin and Collagen I) on 2D polyacrylamide hydrogel substrates and consequently obtain precisely defined cell culture [2](Fig. 1b).
- Demonstration that the metastasis like phenotype of HCT-8 cells is independent of adhesion sub-system [3].

## Future Research

- As the behavior of colon cancer cell is known in 2D cell culture model, a well characterized gelatin methacrylate hydrogels model will be developed to study the influence of matrix stiffness in 3D which resembles more closely the in vivo condition.
- Successful identification and understanding of metastasis-triggering signals is critical for the design of novel anti-metastasis therapeutics and hence for meeting the grand challenge of treating cancer successfully.

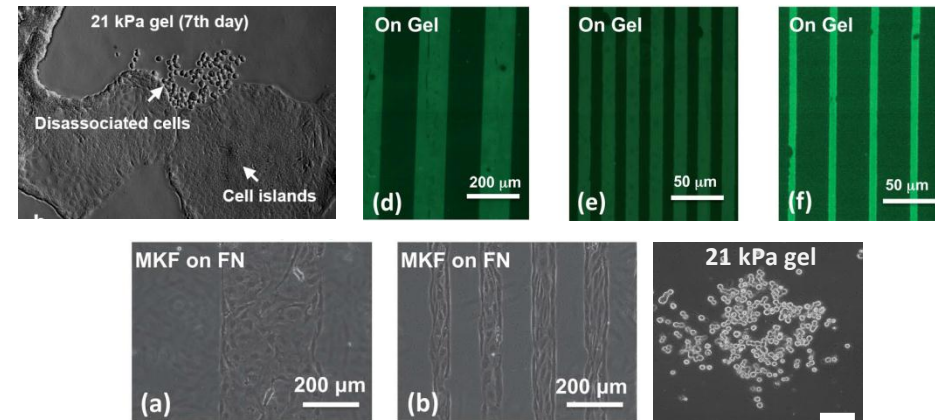


Fig 1 Top (a) HCT-8 cells cultured on intermediate stiffness gel substrates ( $E=21$  kPa, coated with fibronectin) show metastatic-like phenotype (MLP), (d-f) FN patterns on PA gels Bottom (a-b) Cells are cultured on patterned fibronectin on 21 kPa gel substrates. (c) HCT-8 cells show MLP on E-cadherin coated 20 kPa gels as well. Scale bar: 100 μm.

[1] Tang X, ..Kuhlenschmidt MS, Saif TA et al. Biophysical Journal 2010. [2] Tang X, Ali MY, Saif TA. Soft Matter 2012.

[3] Ali MY, Saif TA. Submitted for publication.