Alternating confinement in collagen microtracks *in vitro* influences cancer cell migration

VANDERBILT SCHOOL OF ENGINEERING

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Background

- Metastasis accounts for 90% of cancer related deaths
- During metastasis, cells migrate from the primary tumor, through the bloodstream, and into other areas of the body to colonize and form secondary tumors
- Cancer cell migration through the collagen-rich extracellular matrix (ECM) surrounding the primary tumor is not fully understood
- Because it is known that cells can sense spatial restrictions, it is thought that cells can be conditioned to migrate more efficiently through challenging environments

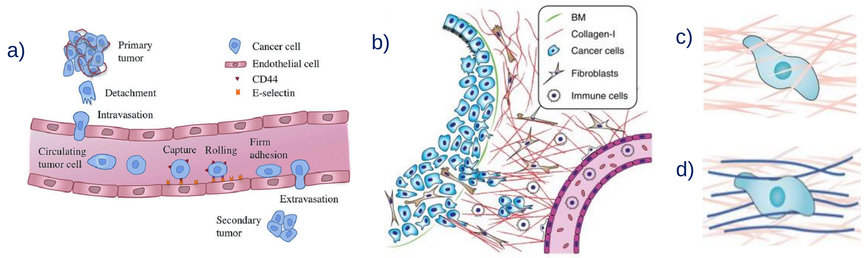

Figure 1: a) Metastatic cascade[1], b) Microenvironment surrounding a tumor *in vivo*[2], c) Disorganized collagen fibers *in vivo*[3], d) Organized "channel-like" collagen fibers *in vivo*[3].

Methodology

- Created collagen microtracks to mimic the ECM of the primary tumor
- Designed microtracks of alternating width to test the hypothesis of cellular "mechanical memory" during migration
- Etched microtrack pattern onto a silicon wafer via photolithography
- Created PDMS stamps from wafer
- Stamped PDMS into collagen to form microtracks
- Seeded MDA-MB-231 breast cancer cells into microtracks and capped tracks with collagen lid
- Allowed cells to migrate for at least 12 hours and tracked their movement

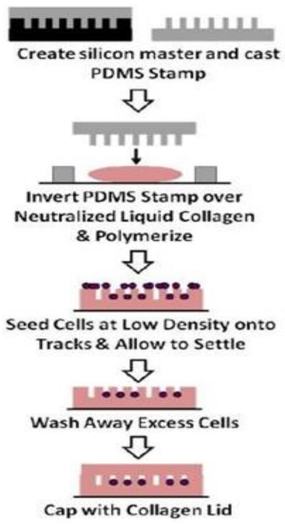

Figure 2: Process of making collagen microtracks *in vitro*[5].

Results

- Microtracks of either 7 μm or 15 μm in width were fabricated to monitor cell migration as controls
- Repeated confinement was investigated using microtracks of width alternating between 7 and 15 μm.

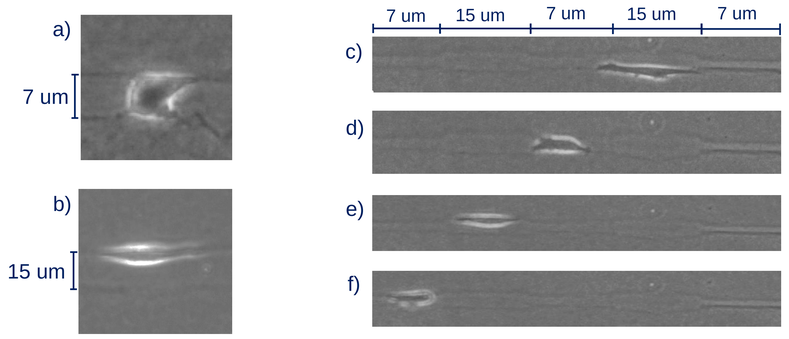

Figure 3: a) Full confinement in narrow microtracks, in which the cell touches all four surrounding walls, b) Partial confinement in wide microtracks, in which the cell touches three or fewer walls, c-f) Images of a cell migrating through wide (c and e) and narrow (d and f) sections of an alternating width microtrack.

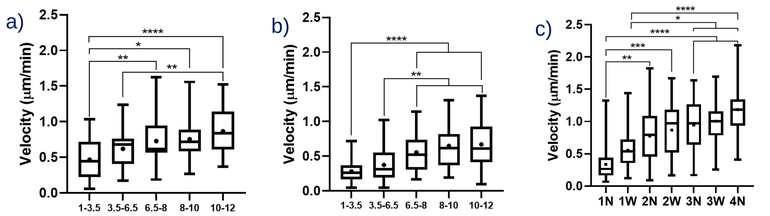

Figure 4: a) Increasing velocity over time as cells migrate through 7 μm microtracks and b) through 15 μm microtracks, c) Increasing velocity through multiple sections of alternating width microtracks, with 1N indicating the first narrow section a cell travels through, 1W indicating the first wide section, and so on.

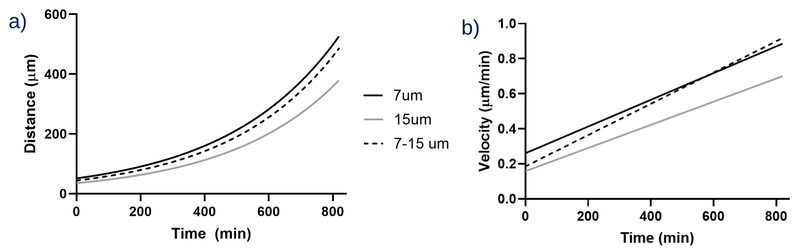

Figure 5: a) Graph of distance traveled by cells over time in microtracks of 7 μm, 15 μm, or alternating width fit to an exponential curve, b) Graph of velocity of the cells over the same period of time fit to a linear curve.

Conclusions

- Cells do not move farther in microtracks of alternating width compared to uniform width, indicating that they are not conditioned to move faster upon encountering repeated confinement as hypothesized
- However, in microtracks of alternating width, cells attain higher final speeds than they do in uniform width tracks, indicating that they accelerate more
- Future work will explore more extreme degrees of confinement, in microtracks alternating between 5 and 20 μm in width to ensure that cells are either fully confined or partially confined to determine the impact on speed

References

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