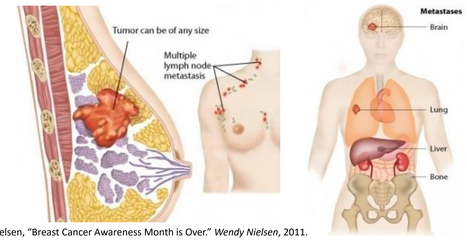
Design and Fabrication of a Stabilizing Apparatus to Efficiently Profile the Relative Adhesive Signature of Metastatic Cancer Cells

Nguyen Nguyen, Emily Gosti, Harsha Kittur, Maxwell Johnson, Dino Di Carlo
Department of Bioengineering, University of California - Los Angeles

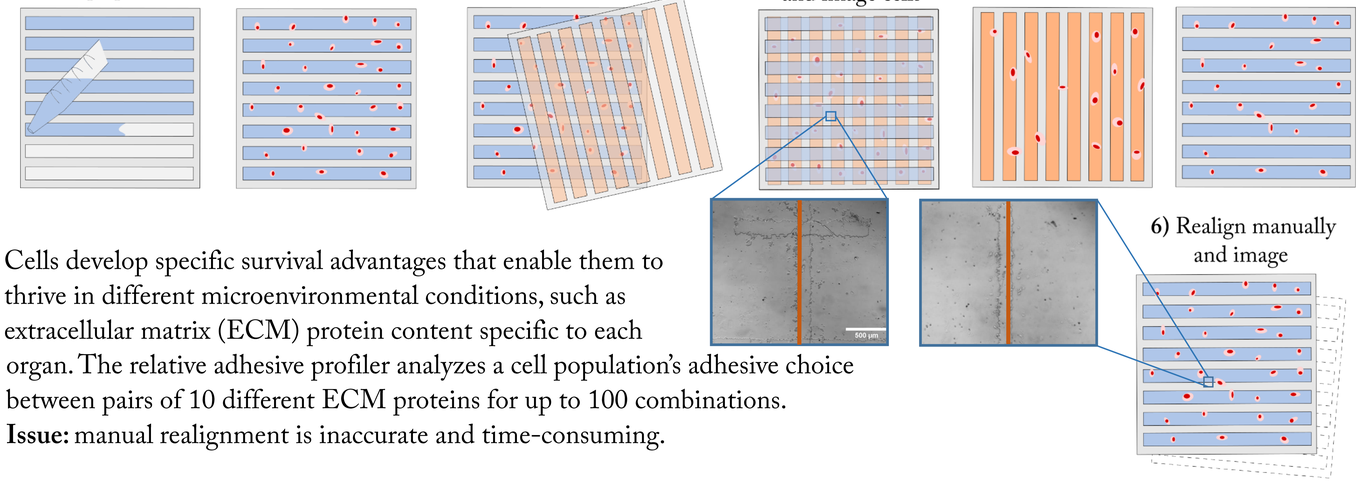
Breast cancer mortality is attributed to unpredictable metastases

Over 40,000 women die of breast cancer in the US, mostly due to untraceable and aggressive migration of the cancer to various regions of the body. While genetic markers are powerful indicators of metastatic risk, they are insufficient for accurate diagnosis. We aim to support these genetic markers with physical adhesive-based markers.



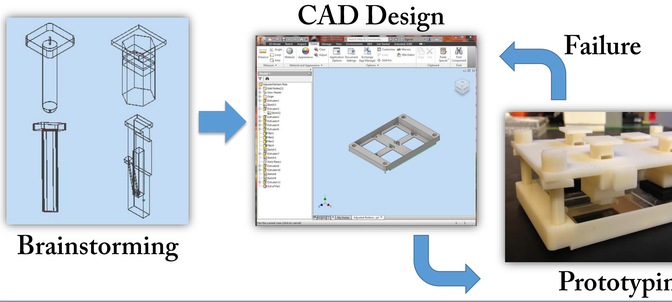
W. Nielsen, "Breast Cancer Awareness Month is Over." *Wendy Nielsen*, 2011.

Relative adhesive platform distinguishes metastatic cell populations



Cells develop specific survival advantages that enable them to thrive in different microenvironmental conditions, such as extracellular matrix (ECM) protein content specific to each organ. The relative adhesive profiler analyzes a cell population's adhesive choice between pairs of 10 different ECM proteins for up to 100 combinations.
Issue: manual realignment is inaccurate and time-consuming.

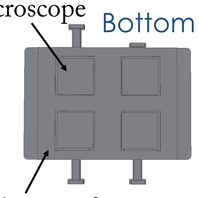
Design and fabrication of alignment device



Design constraints:
1) Platform matches microscope stage dimensions
2) Separation of slides retains x and y coordinates
3) User-friendly and efficient

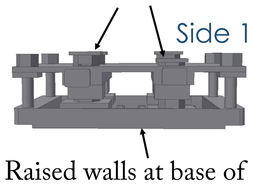
Adhesion pattern profiling stabilization apparatus (APPSA)

Four square cutouts for imaging with inverted microscope



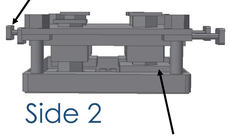
Glass bottom for a transparent base that holds media and PDMS

Hexagonal poles have two positions:
Up – slides separated
Down – slides compressed



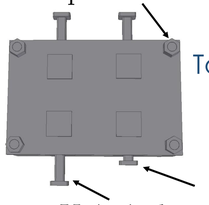
Raised walls at base of device to contain media for cells

Locks slides in x and y position, moves in z direction



Attachments printed in black to minimize fluorescent interference

Nut and bolt ensure stability and enable top plate removal

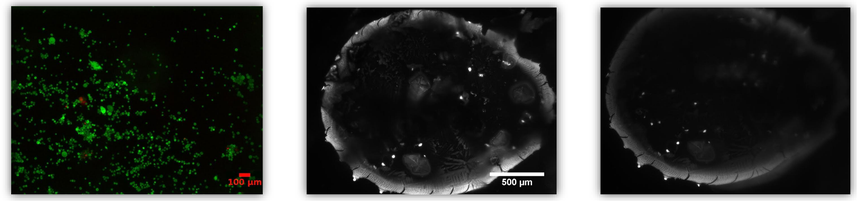


Unlocked position

Locked position

Old and new methods support adhesion profiling to distinguish between lung and brain metastasizing cells

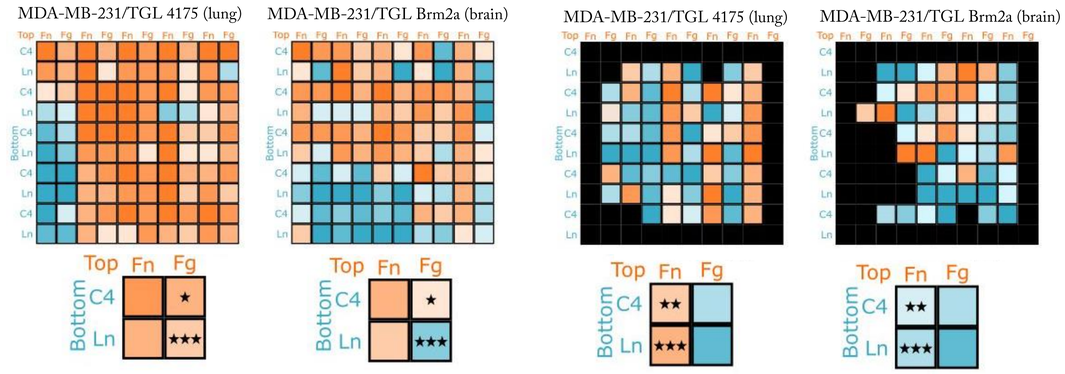
APPSA is capable of 98% cell viability and keeps plates aligned after separation



Live (green) and dead (red) cells

Fluorescent protein dye before (left) and after (right) separation of plates

Testing for significant differences between lung and brain



Taking the average percentage transferred for each protein combination, we detect a significant difference between lung and brain metastasizing cells in half of the combinations for both the old and new device.

★ = $p < 0.1$
★★ = $p < 0.05$
★★★ = $p < 0.01$

0 10 20 30 40 50 60 70 80 90
Percent transfer to top surface

User-friendly APPSA system can unearth physical biomarkers for cancer identification

The reliability of the new device was compromised due to leaks during the experiment, which resulted in heavy cell loss. However, the APPSA system is a novel way to image the adhesion patterns of metastatic cancer cells, able to eliminate the inefficient alignment step. In the future, APPSA can be automated to further increase imaging speed and consistency. The accessible nature of the design enables commercialization of the device. This technology will aid in profiling the adhesive landscapes of cancer cells, which may predict cancer metastatic destinations.

Acknowledgements

We would like to thank Harsha Kittur for his endless support and for letting us adopt his project during this program. Thank you to Maxwell Johnson for guiding us through the process of starting and completing a project. William Herrera, Luke Shaw, and HSSRP also deserve our thanks for providing us with this unforgettable opportunity. Lastly, we would like to acknowledge the Di Carlo Lab for lending us its facilities and for providing an encouraging and collaborative environment for us to work in. All cells were received as a gift from USC Professor Min Yu's lab.

2015 High School Summer Research Program

UCLA ENGINEERING
Henry Samueli School of Engineering and Applied Science
Birthplace of the Internet