In Vitro Disease Models

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Executive Summary

•Electrospinning is a cheap, non-clean room method of preparing nanofiber meshes for cell culture, tissue engineering, medical devices, and drug screening applications

•Mechanical properties and geometry tailorable to desired end uses

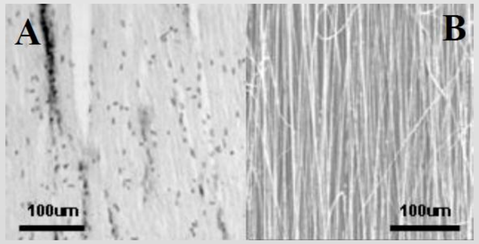
•Easily incorporate both natural and synthetic polymers as well as chemical cues, growth factors, etc.

•Three-dimensional (3-D) cell culture mimics the *in vivo* topography

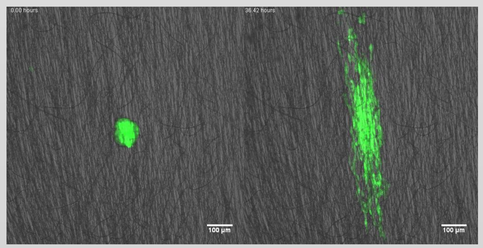
Results: High-Throughput Migration Assay

• Cells on aligned fibers migrated at an effective velocity of 4.2 ± 0.39 µm/h compared to 0.8 ± 0.08 µm/h on random fibers, closely matching *in vivo* models and prior observations of glioma spread in white versus gray matter.

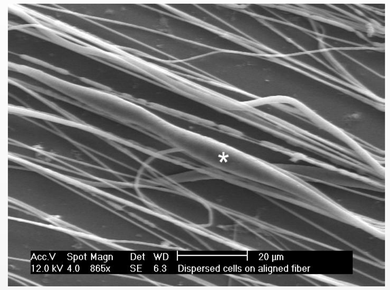
• Glioma stem cell–containing neurospheres seeded on random fibers did not show cell detachment and retained their original shape; on aligned fibers, cells detached and migrated in the fiber direction over a distance sixfold greater than the perpendicular direction.

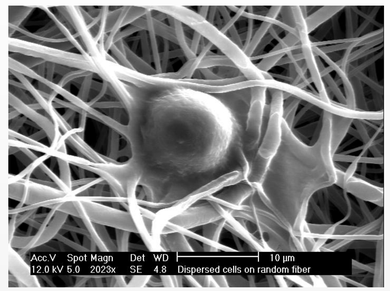


• (A) confocal image of aligned white matter in the corpus callosum and (B) aligned nanofibers from electrospinning (scanning electron microscopy). The latter closely mimics the *in vivo* topography/alignment.

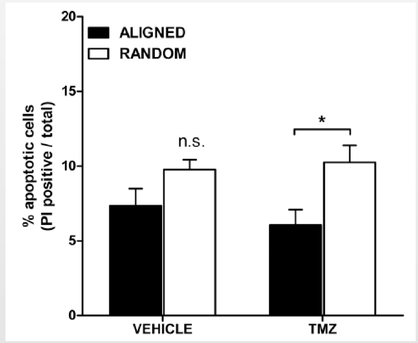


• Initial (left) and 36hrs later (right) of a GFP labeled human glioma neurosphere demonstrating migration/metastasis of tumor cells along aligned electrospun fibers. Fibers aligned vertically.





• Scanning electron microscopy showing examples of isolated U251 human glioma cells migrating on aligned (left, notice cell denoted with asterisk) or randomly oriented (right) PCL fibers.

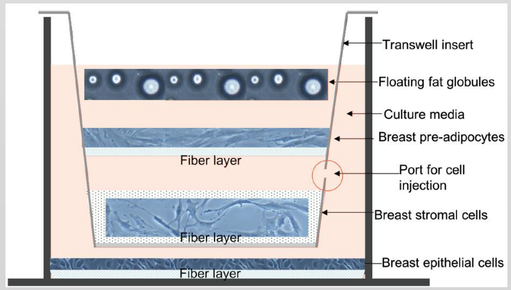


• Percentage apoptotic cells on aligned versus random fiber following temozolomide (TMZ) (400 µM) treatment. PBS only (control) displayed no significant difference.

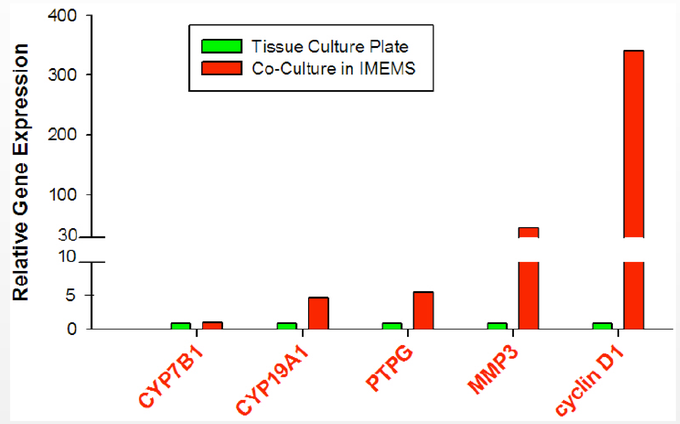
Results: Interactive MicroEnvironMent System

• Significant differences (up to 340 fold increases) in gene expression from primary human normal and cancerous cells grown on flat, tissue culture polystyrene (TCPS) versus cells grown on 3-D nanofibers

• Drug sensitivity/dosage is different for cells cultured on TCPS versus 3-D nanofibers



• Schematic of the Interactive MicroEnvironMent System (IMEMS) which allows co-culture of multiple cell types to provide more realistic culture conditions.



• Relative gene expression of CYP7B1, CYP19 A1, PTPγ, MMP3 and Cyclin D1 in primary normal human breast epithelial cells cultured on the bottom layer of a 4-component IMEMS containing fat globules, stromal cells, and pre-adipocytes exactly as shown in the schematic.

Potential Commercial Applications

- **High-throughput drug screening**
- **Investigation of cancer metastasis and invasion**
- **Multi-cellular co-culture**
- **3-D engineered scaffolds to simulate specific target organs**
- **Bioactive coatings and chemical cues**
- **More accurate drug testing = shorter time to market**
- **More realistic cell culture and testing**
- **Stem cell expansion**

Patents

- **J. Lannutti, J. Johnson, J. Pinzone, M. Ringel, S. Lawler, E. Chiocca, "Low-Cost High-Volume Multi-well Electrospun Substrates," May 2009, provisional patent application filed with OSU TLC**

- **J. Lannutti, J. Johnson, Y. Lin, "Interactive Microenvironment System," June 2009, provisional patent application filed with OSU TLC**

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