Development of a Three-Dimensional (3D) Bioprinted Experimental Model of Rhabdomyosarcoma

Ahsen Haroon[1,2], Phil Imasuen[1,2], Emily Turner-brannen[2], Adrian West[1,2,3]

[1]University of Manitoba, [2]Childrens Hospital Research Institute of Manitoba, [3]Department of Physiology and Pathologyphysiology

INTRODUCTION

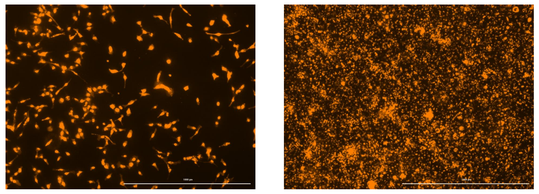
- Rhabdomyosarcoma (RMS) is a childhood cancer of the skeletal muscle and is the most common soft-tissue sarcoma
- Treatments for RMS are available, the 5 year can be as high as 90%, but survivability can be as low as 20% in metastatic tumors
- With current 2-dimensional models it is difficult to study metastatic RMS since 2D models do not replicate the physical environment which modulates metastasis
- **Objective: Create a more lifelike model of RMS using novel 3D bioprinting technology.**

METHOD

- RMS cells (aggressive RH30 or less aggressive A204) were stained with a fluorescent cell tracker dye (1-5 µM) and imaged for several days to confirm the feasibility of long-term observation
- Using 3D bioprinting, a cellular ring of C2C12 myoblasts was printed in an alginate/collagen/fibrinogen bioink
  - Pre-stained RMS cells were mixed heterogeneously into C2C12 cells before printing (5% RMS cells),
  - Or were inserted as a spot tumor during the bioprinting process.
- Bioprinted constructs were imaged daily by live-cell microscopy.

RESULTS

Cell Tracker Dye day 1 (right) and day 6 (left). Cells retained the dye.



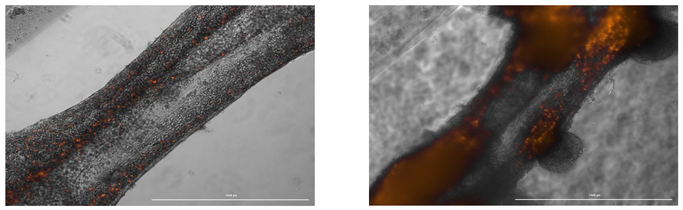
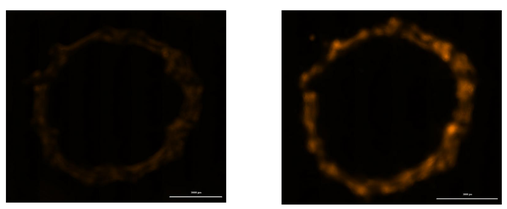
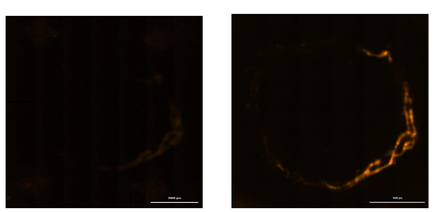


Image of RMS cells and muscle cells, on day 1 (right) and day 13 (left)

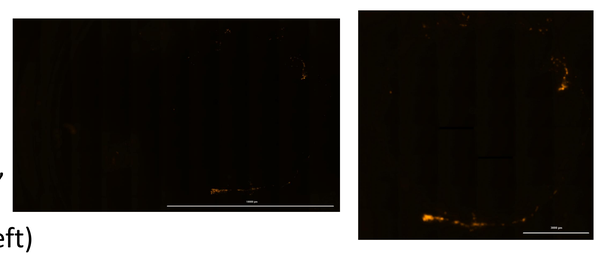


Montage of RMS cells printed heterogeneously with C2C12 myoblast cells, day 1 (right) and day 13 (left)

Montage of RH30 cells inserted as spot tumors, day 1 (right) and day 7 (left)



Montage of A204 cells inserted as spot tumors, day 1 (right) and day 7 (left)



DISCUSSION

- Staining RMS cells works, and they can be tracked for at least two weeks
- Can Create diffuse tumors or insert them in specific spots
- RMS cells, both RH30 and A204 were metastatic in the rings
- RMS cells proliferated rapidly (as expected from cancer cells), and RH30 cells were more aggressive than A204 cells (as expected)

Future Experiments:

- New strategies for creating more dense tumors
- Test the response of bioprinted RMS cells to mitogen to simulate disease and to chemotherapy drugs to simulate treatment

ACKNOWLEDGEMENTS

Adrian West

Emily Turner-Brannen

Phil Imasuen

Lumiere Parrenas

Saeid Ghavami

Javad Alizadeh