Developing a 2D in-vitro bone model for cancer metastasis

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NANYANG TECHNOLOGICAL UNIVERSITY

URECA
Undergraduate Research Experience on CAmpus

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Developing a 2D in-vitro bone model for cancer metastasis

Introduction

Cancer metastasis is the spreading of cancer cells to a secondary site. Bone is often the target site for breast and prostate cancer metastasis, afflicting more than two-thirds of patients.

The process of metastasis is represented as follows:

Intravasation
Cancer cells enters lymphatic system from primary tumor site.

Circulation
Cancer cells circulate in blood stream

Cell arrest
Cancer cells stop moving at secondary site and exit the blood vessels into surrounding tissue.

Proliferation
Cancer cells form micro-metastases at secondary site

Complications arising from the disease include cancer recurrence, fractures and pain.

Problem

Cellular interactions in bone metastasis are poorly understood due to lack of adequate disease models.

Objective

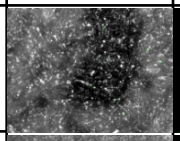
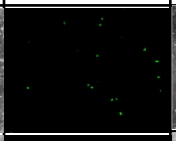
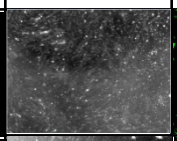
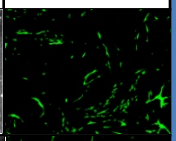
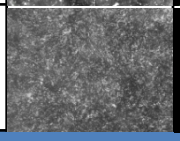
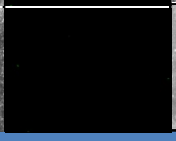
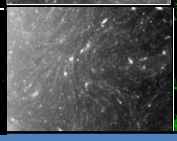
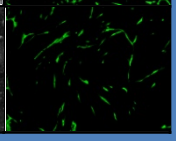
Develop an in vitro model of vascularised bone tissue, osteogenic (bone-forming) mesenchymal stem cells (MSC) and vasculogenic (blood vessel-forming) endothelial cells (EC). Prostate cancer cells will be added to these organotypic cultures to study metastatic proliferation

Method

Culture parameters were optimised to generate vascularised bone tissue. These include
1)Culture medium constituents
2)Cell seeding numbers and ratios
Prostate cancer cells were added to the cultures and subsequently monitored for (a) localisation (b) migration and (c)proliferation

Preliminary Findings

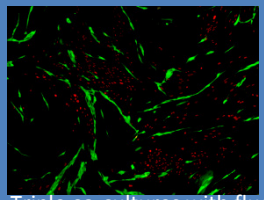
Effect of culture medium (i)

	Osteongenic medium		Vasculogenic medium	
	Brightfield	GFP (EC)	Brightfield	GFP (EC)
Day 4				
Day 8				

Observations
- Culture in osteogenic medium (i) yields mineralised bone tissue but (ii) does not support EC viability
- Culture in vasculogenic medium (i) yields robust networks but (ii) unable to generate bone
- → Further optimisation required

Ongoing work

- Generation of MSC-EC-PC3 (prostate cancer) triple co-cultures (right)
- Evaluation of prostate cancer migration and proliferation



Triple co-cultures with fluorescent labels to facilitate monitoring of indivdual cell types

Project Title: Tissue Engineered Bone Models of Cancer Metastasis
Supervisor: Dr Chong Seow Khoon, Mark