

Primary Supervisor: Dr Beth Coyle

Project Title: Modelling evolution of metastasis in paediatric medulloblastoma using tailored 3D biomatrices

Description: Medulloblastoma, the most common malignant paediatric brain tumour, accounts for 25% of paediatric brain tumour cases. Metastasis is the most important clinical predictor of poor outcome in medulloblastoma. Approximately 30-35% of children present with metastatic disease, seen as leptomeningeal spread via the cerebrospinal fluid. The mechanism whereby tumour cells evolve and disseminate away from the site of the primary tumour is very poorly understood due to the rarity of metastatic samples. As a result, little is known about the intrinsic and extrinsic mechanisms that underlie the metastatic process. Metastatic medulloblastoma is refractory to current treatments, hence there is a need to identify biomarkers that could be used to detect metastatic potential, and more importantly be targeted therapeutically.

The tumour microenvironment is produced by non-tumour cells that are genetically stable and less prone to acquire resistance in response to therapeutic interventions and as such is a recognised therapeutic target in many different cancer types. In order to study the role of the tumour microenvironment in metastatic evolution we must be able to gain an accurate picture of what is present and be able to create in vitro models that can be tailored to represent it. Importantly, these must be

- able to support long-term culture of cells in order to allow cells to achieve full metastatic potential
- amenable to high-throughput analyses so more than a handful of factors and drugs can be studied
- cheaper and more accessible than the current animal models

The aim of this project is to develop an alginate bead based system that can achieve all three of these aims.

Key words: Metastasis, cancer stem cells, multidrug resistance

Fees: High cost laboratory-based research

Please email a CV with a covering letter to Dr Beth Coyle (beth.coyle@nottingham.ac.uk).