Plan Overview

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Title: Utilising tissue-on-a-chip technology as an ex vivo model of breast cancer metastatic colonisation

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Funder: Medical Research Council (MRC)

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Project abstract:

This proposal is for a 12 month NC3Rs Skills and Knowledge Transfer Grant, to transfer existing tissue-on-a-chip technology from the University of Hull, for use as an ex vivo model of cancer metastasis at the University of Manchester. Current metastasis studies mainly rely on in vivo models, however there are well-documented limitations to these for studying cancer cell colonisation, including the large numbers of mice required for longitudinal studies, where animals are culled at specific time points to determine the extent of metastatic colonisation. In vitro/ex vivo models offer an opportunity to reduce the number of mice used in metastasis research. However, to date, a suitable model which incorporates both the whole tissue architecture of the metastatic site along with a physiological arrival of cancer cells via the bloodstream has not been developed. The objective of this project is therefore to create a robust ex vivo model of metastatic colonisation, which accurately models the physiology of cancer cells arriving in metastatic sites. In doing this, and encouraging uptake by the metastasis community, we will significantly reduce the number of mice used in research. In this project we plan to adapt tissue-on-a-chip, an established technology developed at the University of Hull, to a new application for metastasis studies. This technology is the only ex vivo model in existence which incorporates whole tissue pieces with microfluidic channels and pressure driven flow, and has been extensively utilised to study both normal and tumour tissue, but has not been tested for metastasis research.

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Utilising tissue-on-a-chip technology as an ex vivo model of breast cancer metastatic colonisation

0. Proposal name

0. Enter the proposal name

Utilising tissue-on-a-chip technology as an *ex vivo* model of breast cancer metastatic colonisation

1. Description of Data.

1.1 Type of Study

This is a laboratory study which transfers existing tissue-on-a-chip technology created at the University of Hull for use as an*in vitro* model of metastatic colonisation at the University of Manchester.

1.2 Types of Data

Data generated in this project will all be from laboratory experiments. This includes quantification of breast cancer cells colonising mouse liver, immunohistochemical and immunofluorescence analyses of tumour cells, lactate dehydrogenase readouts from liver tissue, images of calcein and PI staining, fixed liver tissue blocks.

1.3 Format and scale of the data

This is a 12 month, small scale project, therefore the amount of data generated will be relatively small. To enable long term accessibility and validation, data will be stored in formats that are open, non-proprietary, and in common use by the research community. All numerical data will be stored as Excel files, and all images will be stored as JPEG files. Slides stained using multiplex immunofluorescence analysis will be scanned within the CRUK Manchester Institute and then saved as JPEG files.

2. Data collection / generation

2.1 Methodologies for data collection / generation

Data will be generated from imaging studies, analysis of histological data, and assays to quantify lactate dehydrogenase output from liver tissue. This data is generated routinely within the CRUK Manchester Institute, and data is collected according to local Standard Operating Procedures across core facilities. All data will be stored electronically as images or databases.

2.2 Data quality and standards

Quality of data will be ensured by all lab members, through use of standardisation and optimised experimental methods, and use of quantitative measures for outcomes wherever possible. Consistency and quality of all data will be controlled by good experimental design, biological replicates, and statistically robust design. All data will be internally peer-reviewed rigorously prior to submission for publication.

3. Data management, documentation and curation

3.1 Managing, storing and curating data

All electronic data are stored and backed up daily on secure University of Manchester (UoM) servers. The project will make use of the UoM Research Data Management Service (RDMS). The RDMS allows researchers to store, manage and curate their data, as well as preserve data after project completion. The RDMS will also cater for publishing and sharing of research data. At the end of this grant, hardcopy laboratory notebooks will be stored securely in the co-applicant (Dr Rachel Eyre's) laboratory for a minimum of 10 years.

3.2 Metadata standards and data documentation

Metadata will be comprised of the following:

- Contextual information about the tissue-on-a-chip in vitro model, collection of data and control mechanisms applied.
- Documented protocols, experiments and results.

All metadata will be recorded as above.

3.3 Data preservation strategy and standards

All data will remain in possession of the University of Manchester (UoM). Relevant research outputs will be retained in the UoM RDMS in alignment with the MRC guidelines on retention of research outputs (minimum 10 years). All data stored on the UoM RDMS will be replicated. Hardcopy laboratory notebooks will be stored securely in the Co-Applicant Dr Rachel Eyre's laboratory for a minimum of 10 years.

4. Data security and confidentiality of potentially disclosive personal information

4.1 Formal information/data security standards

N/A

4.2 Main risks to data security

N/A

5. Data sharing and access

5.1 Suitability for sharing

Data will be suitable for sharing once confirmed and validated. We acknowledge and support the MRC policy on data sharing, which is essential for expedited translation of research into products, intervention strategies, procedures and policies to improve human health and welfare. Data will be made available to the public and other researchers for scrutiny. However we will withhold data until results have been validated, presented at conferences and published in peer-reviewed journals.

5.2 Discovery by potential users of the research data

In due course, all data will be passed to the public domain in the form of open access publications and presentations at international conferences. However, we reserve the right to retain unpublished data within the group until sufficient repeats and validations have been conducted for its meaningful analysis and publication. Published data will be made available through the UoM eScholar repository and the Manchester Cancer Research Centre website. Published outputs will be assigned a DOI (Digital Object Identifier) which can be used to reference the data in publications. Appropriate metadata will be published with the research data to enable other researchers to identify whether the data could be suitable for their own research.

5.3 Governance of access

UoM has a ratified Research Data Management Policy which outlines the governance of access to research data – clearly defining responsibilities. The principle investigator will make the decision on whether to supply research data to a potential new user. Research data will be deposited in the UoM RDMS and published via the UoM eScholar repository.

5.4 The study team's exclusive use of the data

The following is an excerpt from the University of Manchester Research Data Management Policy which is the intended approach of this project:

The University expects its researchers to make Relevant Data openly available to other researchers in a timely way, with as few restrictions as possible. It is recognised that some restrictions may be necessary, e.g. to protect intellectual property, respect confidentiality, or honour third party agreements, but these should be minimised as far as is practicable. It is also recognised that it may be appropriate to allow a limited period of privileged access to the data for the research team that acquired or created it.

We will make data available to other researchers. However, we reserve the right to not share data until we have published/gained the required validation and impact.

5.5 Restrictions or delays to sharing, with planned actions to limit such restrictions

We do not envisage any unnecessary delays in data sharing where experimental data have been validated and have reached the impact required for publication. Thus, we will make data available to other researchers and clinicians, only reserving the right to refrain from publishing until that point. In due course, all data will be passed to the public domain in the form of open access publications and presentations at international conferences etc. However, we reserve the right to retain unpublished data within the group until sufficient repeats and validation have been conducted for its meaningful analysis and publication.

5.6 Regulation of responsibilities of users

Where we engage with commercial or other collaborators, and where appropriate, we reserve the right to share the data and analysis under Non-Disclosure Agreement.

6. Responsibilities

6. Responsibilities

Dr Rachel Eyre (co-applicant) together with Prof John Greenman (the Principal Investigator) will take responsibility for all data, and lodging data with the RDMS as necessary. The PI will have overall responsibility for the quality of the data required, and its storage.

7. Relevant policies

7. Relevant institutional, departmental or study policies on data sharing and data security

Policy	URL or reference
Data Management Policy and Procedures	http://www.miss.manchester.ac.uk/?page_id=425
Data Security Policy	http://documents.manchester.ac.uk/display.aspx?DocID=6525
Data Sharing Policy	http://www.miss.manchester.ac.uk/?page_id=425
Institutional Information Policy	
Other	
Other	

8. Author and contact details

8. Author of this Data Management Plan (Name) and, if different to that of the Principal Investigator, their telephone & email contact details

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