**Convergence Science Centre**

Multidisciplinary Discovery Research Theme

**Cancer Organoids – Expressions of interest**

**Introduction:**

Developing research at the convergence of the clinical, engineering, physical and life sciences is the key focus of the [CRUK Convergence Science Centre](http://www.convergencesciencecentre.ac.uk/) at the ICR and Imperial College. Following consultation and engagement within the research community, the Centre has identified the field of cancer organoids as an opportunity area in its Multidisciplinary Discovery Research Theme for combining engineering and physical sciences expertise with cancer biology to advance our understanding of fundamental cancer processes. We are seeking expressions of interest to contribute to the development of research proposals that address specific priority areas for the furtherance of cancer organoid models in cancer research and treatment (see below). Researchers will have access to Centre funded infrastructure to bolster the scope of their project proposals (see below). The primary intention is to support cancer organoid research that allows generation of the preliminary data required to build a more substantive project or programme that could attract funding from external sources, for example the [CRUK Multidisciplinary Project Award](https://www.cancerresearchuk.org/funding-for-researchers/our-funding-schemes/multidisciplinary-project-award) or [Wellcome Trust Collaborative Award](https://wellcome.org/grant-funding/schemes/collaborative-awards-science).

**Scope:**

A long term aim of the Centre is to extend the use and utility of cancer organoid models to accelerate progress in the study and treatment of cancers of unmet need. Initially, we would like to focus on specific topics that have the potential to make significant impact on the relevance of such models to patient disease. **These topics are as follows:**

## Improving derivation rates for patient-derived cancer organoid models

Before patient-derived cancer organoid models can be used routinely for personalised medicine, a number of hurdles need to be overcome. Current cancer organoid propagation techniques have a significant failure rates which can have varied causes. For lung cancer organoids, overgrowth of healthy cells can outcompete cancer cells leading to their loss from the model system. It has been estimated that less than 20% of organoid cultures derived from lung cancer samples contain cancer cells. For some tumour types (e.g. breast cancer), optimal organoid growth conditions are unknown leading to either bias in the genetic subtypes that can be represented or a complete failure to establish any organoid models. For other tumour types (e.g. pancreatic cancer), differential growth rates can be observed under identical culture conditions suggesting that additional factors may be influencing culture viability. To address these limitations in the establishment of organoid cancer models, we would like to identify researchers with relevant skills for the determination of optimal growth conditions for hard to culture tumour types. Factors that could be considered include, but are not limited to:

* Growth factor screening and more sophisticated delivery
* Tumour heterogeneity/cancer-associated fibroblasts – supporting growth of hard to culture tumour cells as part of a co-culture system with mixed cell populations
* Artificial 3D matrix development – including the ability to support imaging (e.g. minimisation of intrinsic fluorescence)
* Incorporation of nutrient and O2 gradients
* Scalability, reproducibility and cost-effectiveness of new methods

It is the intention that long-term support will be provided to integrate new matrix/growth culture methodologies and approaches into the centre organoid facility to expand the range of tumour types that can be grown as organoids.

## Cancer organoid co-culture and tumour microenvironment (TME) model systems

Cancer organoid models represent a step change in the ability to study cancer cell interactions and behaviour in the laboratory. However, cancer organoid models comprising solely of cancer cells do not adequately represent the complex multi-cell populations of a tumour nor the physical and biochemical properties of the tumour microenvironment. We would like to support the development of more sophisticated cancer organoid models which more closely resemble cancer cell ‘habitats’ found in disease *in vivo*. Parameters that could be considered are:

* Extracellular matrix composition and mechanical properties
* Controlled and reproducible incorporation of other cell types into cancer models e.g. fibroblasts, immune cells
* Tumour heterogeneity – representation of multiple genetic backgrounds within a single organoid model
* Modelling of immune infiltration processes
* Vascularisation and fluid flow around and within a tumour
* Physical forces experienced by tumours e.g. mechanical stresses via normal body movements
* Measurement and control of the physical and biochemical parameters of the model system
* Imaging challenges in complex multicellular models e.g. cell tracking, incorporation of microscopy capability into bespoke culture systems

## 3. Modelling the systemic interactions between a tumour and the rest of the body

Cancers do not develop in isolation. Tumours form within the multiple organ systems of the body and the circulatory and lymphatic networks provide a link from the tumour to every patient tissue. This has many implications for disease progression. For example, immune surveillance relies on this mass transport system to pick up and react to signatures of malignancy. As the disease progresses, the compromise of organ system function can provide challenge to the growing tumour (e.g. reduced blood flow and consequent reduction in nutrient availability) and can lead to the generation of diagnostic biomarkers and symptoms. Ultimately, many cancers undergo metastasis spreading to sites distinct from the original lesion. It is known that cancers can communicate with and influence the behaviour of healthy tissue by the release of nucleic acid messages delivered in the form of extracellular vesicles (EVs). Interdependencies within the body can also impact on treatment – drugs that may be very effective against tumour cells can also damage healthy tissue. In particular, liver and cardiac toxicity can reduce the maximum therapeutic dosage of an otherwise ideal treatment to below efficacious levels. We would like to invite proposals to employ organoids to address problems associated with tumour interactions with distant sites. This could include:

* Interaction with other organ systems e.g. linkage of organoid cancer models to organ-on-chip systems (e.g. liver/heart) to allow prediction of therapy associated toxicity/side effects
* Microfluidic tumour/lymphatic systems for modelling immune presentation
* Extravasation and spread – modelling of metastasis and cancer cell migration, circulation and invasion/colonisation
* Tumour signalling/EV production to “prime” distant sites for colonisation

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**Eligibility**

Expressions of interest for up to £100k are welcomed from individuals or teams who believe that they have relevant skills and experience to tackle the priority areas set out above. Additionally, researchers must confirm that they have access to space and equipment to undertake research and that their contract allows them to undertake an independent research project. Collaborative teams with complementary skillsets will be identified, either by the researchers themselves or with Centre assistance and these must comprise researchers from both Imperial and the ICR. These teams will then be expected to develop mature proposals setting out an experimental route to achieving defined project objectives. Project proposals should include milestone achievements to monitor progress and demonstrate a clear trajectory towards an external funding application. Projects should typically be led by researchers from different disciplines, and while the collaborative teams do not need to be newly formed, the project needs to be novel. Lead applicants will be expected to have equal intellectual input into the design and delivery of the study and will be given equal recognition for the project. Applications are particularly encouraged from newly independent investigators.

**How the proposals will be judged**

Once fully developed, proposals will be ranked using the following criteria:

* Importance of the question to be addressed in cancer or the potential impact of a novel technology.
* Need for a convergence science approach to address the problem – the Convergence Science Centre defines convergence science as research that brings together distinct scientific disciplines to generate new methodologies and technologies that will allow previously intractable questions to be addressed i.e. it will not support projects that are simply applying existing methodologies and technologies to address a problem. For clarity, this excludes collaborations solely between biological disciplines e.g. immunology with genetics or pathology with epidemiology unless there is a clear novel technological aspect.
* Quality of the science proposed – with sufficient experimental detail across all disciplines involved.
* Future plans to develop the project – highlighting how this funding will provide the necessary preliminary data to make the project competitive for external funding. The schemes you are intending to target should be identified.

The applications will be reviewed by the Research Subcommittee of the Centre, which may seek additional internal peer review to make its final assessment.

**Additional Resources:**

The Centre provides [core funded infrastructure](https://www.convergencesciencecentre.ac.uk/research/infrastructure) to support convergence science activity and can support the generation of MTAs as required. Of particular relevance to this funding call are:

Microfabrication and prototyping facility – The Centre provides a microfabrication and prototyping facility, housed at Imperial (South Kensington and White City campuses) for the rapid production of small devices for pre-clinical *in vitro* studies. Supported by a dedicated technician, the facility has access to clean room facilities and a range of equipment for the development of bespoke devices. The facility can be used for the production of, for example, microfluidic devices, organs-on-chip, biosensors, electrochemical sensors, microneedles and others.

Organoid culture and biobank facility – The Centre provides an organoid culture and biobank facility, housed at the ICR (Chelsea) with dedicated technical support. It provides on-site training in the use and propagation of organoid cultures, supports the production of robust and reproducible organoid models and establishes/distributes new clinically annotated cancer organoid models.

More details of these and the other infrastructure facilities/posts available to Centre researchers can be found via the link above.

**Deadlines:**

Expressions of interest should be registered by filling in the short application form below. Completed forms should be sent to icr-imperial-convergence.centre@imperial.ac.uk by 5pm on January 15th.

**CRUK Convergence Science Centre | Cancer Organoids Expression of Interest**

Guidance for filling in this form can be found [here](http://www.convergencesciencecentre.ac.uk/).

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| 1. **Name(s), institutional affiliation and department.** |
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| 1. **Expertise – Describe your expertise that would be applicable to the development of novel cancer organoid models and technologies** |
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| 1. **Ideas – Outline your ideas for convergence science\* projects that address one or more of the cancer organoids priority areas (see guidance). Give an indication of the longer term aims that could form the basis of an external funding application.** |
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| 1. **Additional expertise required – Please detail additional expertise and any equipment requirements to enable such a project to be successful.** |
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| 1. **Costings – Please indicate the approximate costs for equipment, consumables and positions that would be required to initiate the project (max £100k).** |
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**\*Convergence science is defined by the Centre as work that brings together distinct disciplines to produce outputs that could not have been generated in isolation and that could not have been performed elsewhere (e.g. in other CRUK Centres). Projects must contain an element of engineering and/or the physical sciences.**

For help with this form, please contact Simon Pennell ([simon.pennell@imperial.ac.uk](mailto:simon.pennell@imperial.ac.uk)).

Submissions should be emailed to [icr-imperial-convergence.centre@imperial.ac.uk](mailto:icr-imperial-convergence.centre@imperial.ac.uk) by 5pm on the 15th January 2021. Late submissions will not be accepted.