

Results of Competition: Application of Whole Genome Sequencing Approaches to Cancer

Competition Code: 1910_ISCF_ASHN_GEL_CANCERWGS

Total available funding is £5.4m

Note: These proposals have succeeded in the assessment stage of this competition. All are subject to grant offer and conditions being met.

Participant organisation names	Project title	Proposed project costs	Proposed project grant
CAMBRIDGE CANCER GENOMICS LTD	WISDOM - Whole Genome Sequencing and Artificial Intelligence for improving survival in Oesophageal Adenocarcinoma	£690,082	£310,537
Cambridge University Hospitals NHS Foundation Trust		£17,059	£17,059
CYTED LTD		£51,500	£36,050
University of Cambridge		£287,423	£229,938

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Project description - provided by applicants

Awaiting Public Project Summary

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PERSPECTUM DIAGNOSTICS LTD	Integrated whole genome sequencing into care for patients with liver tumours	£699,685	£419,811
Hampshire Hospitals NHS Foundation Trust		£80,032	£80,032
University of Oxford		£216,555	£216,555

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This project aims to improve the clinical care of patients with liver tumours. By developing state-of-the-art tools that integrate genetic, radiology and pathology information we expect to improve the diagnosis and characterisation of tumours, and inform the selection of therapeutic options. This has the potential to improve clinical outcomes for the patient and reduce costs for the healthcare system.

Liver surgery is the treatment of choice for curing liver tumours. However, surgery has inherent risks which are exacerbated if liver health is already compromised. This is of particular concern with the rising prevalence of obesity-linked chronic liver disease and more aggressive pre-operative chemotherapy.

A major opportunity for improving diagnosis and treatment of liver tumours is better characterisation of tumour tissue, liver health and patient physiology. While there have been huge scientific and technical innovations in the understanding of liver and cancer biology, the translation of these developments to bedside care to improve health outcomes for cancer patients has been limited.

Perspectum span out of the University of Oxford to commercialise novel MRI technology for diagnosing liver disease. In this project, Perspectum will collaborate with leading experts at the University of Oxford and Hampshire Hospitals NHS Foundation Trust (HHFT) to deliver this project.

Initially, we will establish the analytical validity and clinical validity of either whole tissue or single cell whole genome sequencing (WGS). We will then begin a prospective study, in which patients can be included, as part of their standard package of care. With this consent Perspectum will provide a detailed consolidated and actionable report containing quantitative MRI imaging, digital pathology and WGS. This report will then be provided to the physician to assess the value of these additional metrics and whether they would have influenced the physician in determining the most appropriate treatment pathway for the patient.

This project will develop a combined WGS, digital pathology and imaging approach to understanding primary and secondary liver tumours in patients with suspected liver cancer. Combining advanced imaging, pathology and WGS is something not currently done in clinical practice. By utilising this integrated approach, we hope to demonstrate measurable improvement in clinical outcomes and substantial benefits for healthcare systems.

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PINPOINT ONCOLOGY LTD	Whole genome sequencing of liquid biopsies to predict doxorubicin response in ovarian cancer	£96,293	£67,405

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Pinpoint Oncology is developing new genetic tests on DNA from tumours to take the guesswork out of treating the deadliest cancers. We use machine learning to find patterns in tumour DNA which can be used to predict a person's response to cancer drugs.

Our current test uses a biopsy of a patient's tumour to predict if they will respond to a drug used to treat ovarian cancer. In this project we want to see if we can use the same test on a patient's blood sample, rather than a tissue sample. If successful, this will be less invasive for the patient, safer, more convenient, and will reduce the cost of the test.

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ROCHE PRODUCTS LIMITED	Carcinoma of Unknown Primary Site (CUP) a comparison across tissue and liquid biomarkers (CUP-COMP)	£460,000	£230,000
Christie NHS Foundation Trust		£205,742	£205,742
CONCR LTD		£241,000	£128,700
Durham University		£90,857	£90,857

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NewCo Limited	Whole Genome Sequence-guided targeting of colorectal and oesophageal cancers	£699,377	£489,564
Wellcome Trust Sanger Institute		£299,462	£299,462

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BASE GENOMICS LIMITED	Base Genomics: A novel method for single-step, ultra-sensitive, combined DNA methylation and mutation detection of cancer from liquid biopsies using WGS	£843,600	£379,620
University of Oxford		£144,761	£144,761

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MY PERSONAL THERAPEUTICS LTD	Personalised therapies based on simultaneous targeting of complex oncogenic networks identified by WGS.	£519,462	£363,623
Imperial College London		£113,167	£113,167

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In theory, to find an efficient treatment for cancer we have only to identify an oncogenic mutation and target it with a well characterized drug. In practice, however, every cancer is driven by multiple mutations occurring in unique combinations, which generate a complex tumour network in each patient. When oncologists have tried to practice single-target precision medicine, promising initial results fade as the full genetic complexity of the tumour is not captured. Although whole-genome sequencing (WGS) offers the opportunity to identify tumour-associated gene mutations, its present utility in personalised cancer therapy is rather limited. To give WGS an effective clinical significance it is essential to use the genomic information to build models that can match cancer patients to the optimum drug mixtures.

My Personal Therapeutics (MPT) use fruit flies (*Drosophila*) and its arsenal of sophisticated genetic tools to model individual patient's tumours features. We reconstruct tumour genetic complexity identified by WGS, in the intestine of flies. These fly "avatars" will develop the patient's tumour and will die by the same cancer, unless they take the right combination of drugs. Then we use these cancer avatar flies to test thousands of approved compounds to identify the best drug combinations that rescue cancerous avatars from lethality. In this way, we produce a precise picture of the interaction between a growing tumour within an entire animal and the drug combinations tested.

Via this method, called Personal Discovery Process (PDP), MPT delivers ultra-personalised drug treatment recommendations for patients with gastrointestinal cancers (GIC), a hard-to-treat malignancy diagnosed for 180 people every day in the UK. In this project, MPT will partner with the London IVD Co-operative, a UK NIHR centre that conglomerate UK top GIC specialists and the best infrastructure to accrue GIC patients. Our process currently takes four to six months and is expensive, making widespread uptake unlikely. In this project, we will create 40 avatar models and produce drug screening data that can be used to train a machine learning tool that will match incoming patient's tumour profile with previous patient's data. In this way, using artificial intelligence, we will achieve a reduction in time taken and cost. This tool will predict the best possible combination therapies and could be widely adopted as part of cancer diagnosis and treatment.

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