ICR The Institute of Cancer Research

Imperial College London

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Project title: Overcoming resistance: Remodelling the Prostate Cancer Microenvironment using Synthetic Cells

Project Summary:

Prostate cancer (PC) is the most commonly diagnosed and second-most lethal cancer diagnosed in UK men, with treatments for inoperable (or recurrent), therapy-resistant PC being the major clinical need. Although hormonal therapies are initially effective, progression to life-threatening castrate-resistant prostate cancer (CRPC) inevitably occurs. The PC tumour microenvironment acts in different ways to drive drug resistance, acting as a fibrotic mechanical barrier that prevents the penetration of drugs into the tumour. This high intratumoral pressure also results in a hypoxic tumour phenotype and reduced infiltration of T-cells, further driving drug resistance. Targeting the PC tumour microenvironment could therefore not only improve the performance of approved small molecule therapies (e.g. docetaxel) but synergise with promising immunotherapies such as checkpoint inhibitors that have to date shown limited effectiveness in CRPC. This multidisciplinary project aims to develop a new approach to treat CRPC by engineering a novel synthetic cell medicine that remodels the tumour microenvironment. This approach exploits enzyme overexpression specific to the PC microenvironment to selectively activate synthetic cells, leading to release of remodelling compounds into the microenvironment that reduce tumour fibrosis. This in turn reduces intratumoral pressure, increasing the penetration of therapeutics throughout the tumour and priming the tumour for further clinical intervention. This project offers a unique opportunity to develop a detailed understanding of both cancer biology (with a focus on the tumour microenvironment) and microfluidic engineering of advanced drug delivery systems. During the project, the fellow will help develop a variety of in vitro, ex vivo and potentially in vivo microenvironment models to test the effects of various remodelling approaches on microenvironment mechanics, signalling and/or immunosuppression. In addition, the fellow will learn how to design, build and test microfluidic devices as a platform to undertake high-throughput synthetic cell engineering. This will drive translation, facilitating future studies on synthetic cell pharmacokinetics/pharmacodynamics (PET/MRI imaging) and triggered-release behaviour across the developed microenvironment models.

Supervisory Team:

Prof Charlotte Bevan (Imperial)

Prof Oscar Ces (Imperial)

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CANCER RESEARCH UK CLINICAL ACADEMIC TRAINING PROGRAMME

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