SoMS Honours Project Opportunity 2022

Mapping cancer cell signalling through single-cell quantitative imaging and machine learning

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Question: Why we need a better diagnostic in advanced Prostate Cancer

- Prostate cancer (PC) is the second-most common cancer in men and a leading cause of cancer deaths globally
- PC is *initially* driven in by Androgen Receptor (AR) signalling (1), meaning it is sensitive to Androgen Deprivation Therapies (ADT) (2)
- **BUT** resistance to ADT arises in almost all patients (3)
- Resistance can be driven by various alternate molecular signalling pathways that promote cancer cell survival, proliferation and metastasis (4)
- Because solid tumour biopsies cannot be regularly repeated to track changes in molecular signalling in each patient, *we need a new diagnostic method to detect which signalling pathway is active in each advanced prostate cancer patient* (5) to eventually guide selection of an optimal targeted treatment (6)

Knowing resistance signalling pathways per patient will allow treatment with targeted therapies

Which resistance signalling pathway is active in each individual patient?
Our Approach: *Liquid Biopsy, Proteomic Microscopy & Machine Learning*

You will access 3 cutting-edge methodologies to measure which signals are driving prostate cancer in individual patients:

1. **‘Liquid Biopsy’** analysis of Circulating Tumour Cells (CTCs) isolated from PC patient blood samples

   - *Medical Oncologists* treating PC patients provide blood samples

   - Patient X pre-ADT-resistance Liquid Biopsy Sample
     - Liquid biopsy
     - CTC isolation
     - Enriched CTCs

2. **‘Proteomic Microscopy’** involves sequential cycles of molecular labelling & imaging to detect multiplexed signalling pathway activities (and other cancer markers) in each and every patient CTC

   - 2a. CTC samples
   - 2b. Automated Molecular Labelling with Liquid Handling Robotics
   - 2c. Automated Imaging with Confocal Microscopy
   - 2d. Multiplexed CTC Data

3. **‘Machine Learning’** for CTC detection, signalling activity mapping and signatures definition to guide targeted therapy selection. VR analytics support data analysis

   - 3a. Image Analysis
   - 3b. Signal activity mapping via Deep Learning variational autoencoder
   - 3c. VR analytics & signalling signature definition
Your Role: *Tune the project to focus on your strongest interests*

- The Cancer Systems Microscopy lab uses advanced automated labelling and imaging of cultured cells and patient-derived cells (such as CTCs) from liquid biopsies *(1)*

- We develop and use automated image analysis and statistical analysis methods to extract insights from image data spanning 1000s of cells *(2)*

- We also develop and use machine learning and AI tools to link quantitative data analyses to patient outcome prediction *(3)*

- You can focus across all or some of these areas, depending on what you are most excited about.