Edinburgh Cancer Research Centre – Multi-modal (Raman) Microscope

The multi-modal microscope at the Edinburgh Cancer Research Centre is a bespoke tool designed to address the needs of many different researchers in different areas. The multiphoton nature allows the microscope to image deeper into samples than a traditional confocal microscope, this is particularly useful when research is translated from cell cultures towards tissue and animal studies. The microscope has been designed to allow in-vivo imaging within animals using optical windows which allow for observation of growing tumours on living animals.

A key design feature of the microscope is its 'label free' imaging. This allows images to be taken without the need to add fluorescent tags to everything that needs visualising. One of the label free techniques is called coherent anti-Stokes Raman scattering (CARS) which allows you to visualise a particular chemical bond. This is typically used to image fat or protein rich content such as blood vessels, neurons, fat stores and cells.

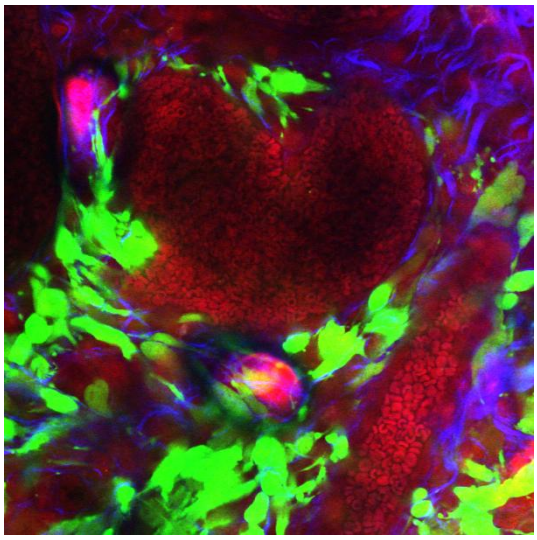

Figure 1 Mouse squamous cell carcinoma. Fluorescent cancer cells (green) can be seen invading past the collagen layer shown in blue and into the blood vessel shown in red. The contrast from the blood and collagen is generated by label free microscopy.

CARS is very useful at looking at cell structures where the chemical bonds in fats and proteins are plentiful. However, to image drugs which may be present in much smaller concentrations requires another type of imaging called stimulated Raman scattering. SRS is a more sensitive variant of CARS that we have currently used to image drugs at millimolar concentrations, and which already out-performs CARS in this regard.

With the recent further help of the **Clerk Maxwell Cancer Research Fund** we have purchased two items that greatly increase the sensitivity of SRS. These are a 20 MHz Electro-optic Modulator and an analogue lock-in amplifier (LIA). The EOM is used to rapidly turn one of the laser beams on and off, and the increase in depth of modulation and frequency over our existing setup will help to increase the sensitivity of this technique as well as the speed. A new LIA that is capable of decoding this signal is also required. Using the new equipment, and working alongside chemists from the University of Edinburgh we expect to see a 10-100 fold improvement in the sensitivity – potentially enabling us to measure micromolar concentrations of important cancer treating drugs. This will help unlock new insights into how cancer drugs are taken up into a tumour, where it resides within cells and how long

it is retained there having biological effect, until it is removed and metabolised. Such resolution and definition will provide a step-change in our understanding of cancer drug pharmacology.