Metabolism is a centrepiece of cancer biology from its initiation, through its progression, to its response to treatment. The facility supports the Institute’s research exploring the multiple roles of metabolism in cancer biology. We offer tailored support for the Institute’s research projects, from experimental design to data analysis. Our well-established metabolomics platform uses state-of-the-art liquid-chromatography mass-spectrometry (LC-MS). Two Thermo Scientific Q Exactive instruments with high-resolution and accurate-mass are central for the targeted and untargeted analysis of the metabolome of cells, tissues, and biological fluids. This platform is complemented by a Thermo Scientific Altis triple quad that broadens the sensitivity and specificity of the detection for specific metabolites of interest. In addition, an Agilent gas-chromatography mass spectrometry (GC-MS) triple quad instrument provides complementary coverage to our LC-MS systems.

The facility’s core aim is to provide access to state-of-the-art LC-MS technology that is optimised for the detection of polar metabolites and lipids. We maintain and operate the instrumentation, providing both standard metabolite profiling and custom analysis when needed. We offer expertise and assistance in data analysis, data interpretation and experimental design. We also offer training in data analysis of targeted metabolomics experiments. To learn as much as possible from the data generated, we collaborate with users to make use of more complex untargeted analysis approaches. We are continuously striving to further develop both our mass spectrometric and data analysis methods.

We work closely with the groups of Saverio Tardito, Owen Sansom, Jim Norman, Sara Zanivan, Vignir Helgason and support several other research groups within the Institute who have specific interests in cancer metabolism.

This year, Engy Shokry joined the facility as a scientific officer. Engy brings a wealth of experience and knowledge in a range of metabolomics techniques which will complement our current methodology. Engy is currently using the facilities GC and LC-MS triple quad instruments to develop novel targeted metabolomics approaches to aid ongoing projects. These include the measurement of methyamine, a volatile derivative of ammonia and the natural substrates and products of 2’-deoxycytidine kinase alongside the metabolites of the drug Cladribine, a nucleoside analogue.

Rachel’s ongoing PhD project in collaboration with Saverio Tardito’s group continues to study the metabolism of BRAF mutant melanoma for therapeutic gain. BRAF inhibitors provide an excellent first line of therapy for melanoma, however, resistance frequently develops. It has been shown that melanoma cells resistant to BRAF inhibitors have increased mitochondrial oxidative metabolism that depends on glutamine anaplerosis. We are using a glutaminase inhibitor in combination with the BRAF inhibitor to assess whether this metabolic rewiring constitutes a therapeutic liability. To identify which metabolic reactions are required by melanoma cells to proliferate upon BRAF and glutaminase inhibition, we are applying targeted and untargeted metabolomics to melanoma cells grown in culture and tumours in vivo.

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