

METABOLOMICS



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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 Exactives instruments with high-resolution and accurate-mass are central for the targeted and untargeted analysis of the metabolome and lipidome 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 MS technology that is optimised for the detection of metabolites and lipids. We maintain and operate the instrumentation, providing both metabolite profiling and custom analysis when needed. We offer expertise and assistance in data analysis, data interpretation and experimental design. We run regular workshops to train users to carry out their own targeted data analysis. To learn as much as possible from the data generated, we also collaborate with users to make use of more complex untargeted analysis.

We work closely with many groups within the Institute who have interests in cancer metabolism and over the past year, we have continued to contribute to their research (see publications). A new and highly successful collaboration with Johan Vande Voorde (University of Glasgow) and Lars Vereecke (VIB Center for Inflammation Research, Belgium) led to the development of a method to measure Colibactin, using a byproduct of its synthesis as a proxy, N-myristoyl asparagine. Which in turn, allowed us to make a meaningful contribution to an important study demonstrating that Colibactin-driven colon cancer requires adhesin-mediated epithelial binding. Another highlight for us this year, was working with Saverio Tardito's group on the

identification of lipids which contain monounsaturated fatty acids and their ability to act as anti-ferroptotic factors when secreted by triple-negative breast cancer cells into extracellular environment.

Over the last few years, biology has been undergoing a spatial revolution and a new generation of technologies are being adopted which has the potential to transform many areas of biological research and pathology. Until recently most omics approaches, could not capture any spatial information, a significant limitation given important biological processes are often driven by a spatial context. Spatial metabolomics is such an innovation, a research field focused on the *in situ* mapping of small molecules – metabolites, lipids and drugs in tissues and organs.

Next year, the facility will begin work on developing mass spectrometry imaging (MSI) as an approach to spatial metabolomics. This was made possible by the successful application and award of MRC Equip funding this year for a MRT (multi reflecting time-of-flight) mass spectrometer. This instrument can uniquely perform spatial metabolomics with two complementary techniques, Matrix Assisted Laser Desorption Ionisation (MALDI) and Desorption Electrospray Ionisation (DESI).

These two methods together will allow us to measure the widest breadth of metabolites possible on the same instrument. We are eager to start developing this technique inhouse and are excited by the possibility of overlaying MSI data with those gathered from many other spatially resolved technologies available in the Institute.

During the summer, the lab also continued the long-standing association with Cold Spring

Harbor labs, assisting in the organisation and practical instruction of the 2024 metabolomics course. The course runs for a period of two weeks, during which the students learn both the theory and application of different GC/LC-MS methodologies to measure metabolism and answer fundamental biological questions in their own research areas.

[Publications listed on page 130](#)

