The Metabolomics facility employs state-of-the-art mass spectrometry techniques to measure small molecules (metabolites) and explore changes in metabolic pathways in cancer cells. The facility supports many cancer metabolism research projects within the Institute. We are also responsible for the analysis of lipids and are currently validating simplified extraction methods for lipidomics analysis. For a third year, we were involved in organising and delivering a practical metabolomics course at Cold Spring Harbor Laboratory in the USA. The team has expanded and a new PhD student studying metabolomics of BRAF mutant melanoma has joined the group.

Our metabolomics platform is currently focused on the use of our two Thermo Scientific LC–MS systems (Q Exactive Plus and Q Exactive) with their high-resolution, accurate mass, Orbitrap technology, used for both targeted analysis and more in-depth metabolite profiling (untargeted). We have well-established LC–MS methods using HILIC chromatography. Our Thermo Scientific™ TSQ Altis™ triple quad mass spectrometer is used for specific targeted LC–MS/MS analysis, offering increased sensitivity and specificity for known metabolites, such as in the measurement of lysophosphatidic acids (LPAs). Our LC–MS systems are complemented with our Agilent Technologies GC–MS/MS triple quad instrument, for measuring compounds such as fatty acids, cholesterol and acetate.

We work closely with the groups of Saverio Tardito, Alexi Vazquez and Jim Norman and also support several other research groups within the Institute who have specific interests in cancer metabolism. We provide advice for sample preparation for a range of sample types including cell extracts, plasma, urine and tumour tissue, and support for data analysis, based on Thermo Scientific™ TraceFinder™ and Compound Discoverer™ software.

With our targeted approach to metabolomics, we have increased the number of metabolites we can identify on our LC–MS platform to 400, which includes a broad range of metabolites of different classes. Potentially all 400 metabolites can be detected in a single analysis. Experiments using stable isotope tracers (such as 13C glucose in the medium) enable us to examine the intracellular kinetics and the proportional distribution of metabolites produced from the tracer. We can also quantify metabolite abundance and calculate metabolite exchange rates between cells and the medium in which they are grown.

Using an untargeted approach, we look for novel metabolic changes, by identifying compounds showing altered abundances in our cancer models. We use Thermo Scientific™ Compound Discoverer™ software, where we can link to other Thermo Scientific™ tools, including their mzCloud™ database of fragmentation spectra. Changes in metabolites can be shown using various statistical approaches, such as PCA and DPLS–DA, and metabolites are identified using a range of factors, such as accurate mass, adducts, isotopes and fragmentation spectra, comparing with the Human Metabolome Database (HMDB) and other databases. We are using this technique for a few specific in vivo and clinical projects.

After Jurre Kamphorst, the lipidomics research group leader, and his group's mass spectrometrist, left during 2018, we have become responsible for all methods for lipid analysis in the Institute.

We are investigating various approaches to lipidomics methodology and data analysis. We have developed a simplified one-phase extraction method and are currently validating this method for cell culture experiments. This methodology shows a good coverage of different lipid species, and allows the use of protein content from the same sample for normalisation. We use high-resolution Orbitrap mass spectrometry (Q-Exactive) in single polarity mode and data-dependent fragmentation acquisition (ddMS2), to identify the lipids using both accurate mass and fragmentation patterns. We apply two complementary approaches for lipidomics data processing. LipiSearch (Thermo Scientific) mainly identifies lipid classes in the sample. For lipid quantitation, our workflow involves a recently developed open-source software called LipiDex, which integrates with Compound Discoverer™ (Thermo Scientific™) software. We use databases such as LipidBlast that contain in-silico fragmentation information for more than 30 lipid classes. The data obtained can be processed using both univariate and multivariate statistics to identify changes in lipid composition in particular biological conditions.

In collaboration with the oncometabolism laboratory, led by Saverio Tardito, our new PhD student is aiming to identify metabolic targets in BRAF mutant melanoma through comprehensive metabolomics. In particular, we are interested in the metabolic reactions which are critical for the development of resistance to BRAF inhibitor drugs. Melanoma patients who acquire resistance to BRAF inhibitors eventually relapse, and novel therapeutic options are needed to impair the progression of these tumours.

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