

Mass Spectrometry @ MDC

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Get in touch!

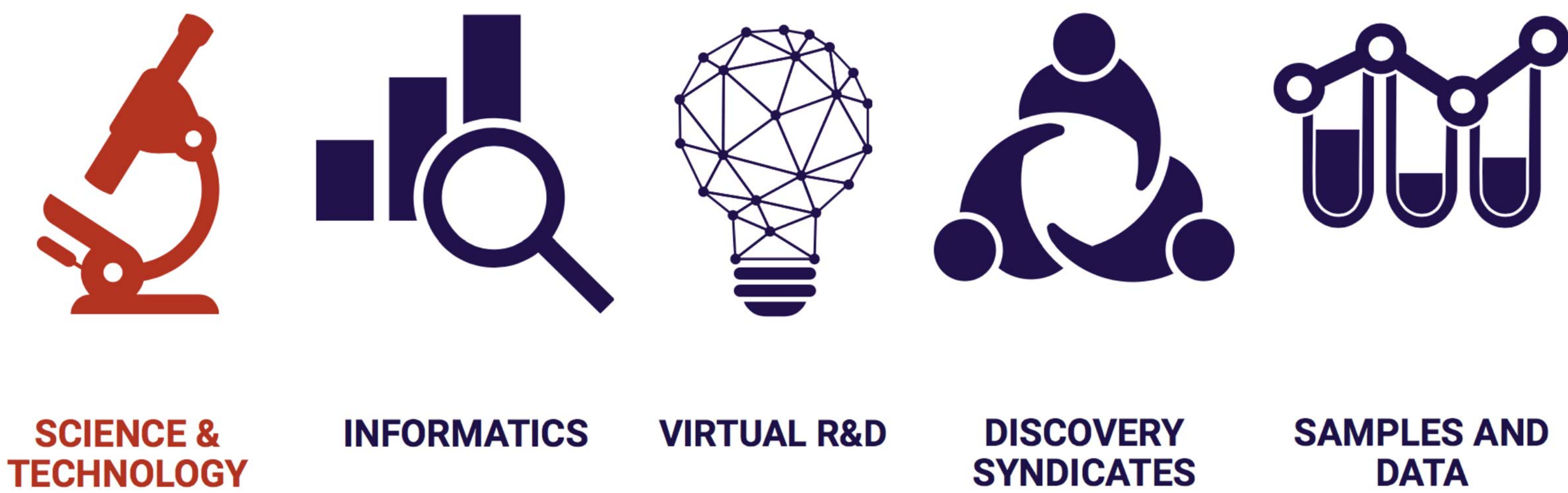
CATAPULT
Medicines Discovery

Funded by

Innovate UK

MEDICINES DISCOVERY CATAPULT

MDC is a national centre for **collaborative R&D** exploring and developing **new approaches** to the discovery and proof of well targeted medicines, diagnostics and biomarkers. Funded by Innovate UK, we are an independent **not-for-profit** company bringing together a fragmented UK sector of industry, academia, charities, technologists, services, finance companies, SMEs and start-ups who together can turn good science into new, high-value products.



MS LANDSCAPE @ MDC

We are establishing an **innovative MS laboratory** accessible to UK SMEs and aiming to **advance medicines discovery** using mass spectrometry as a key technology. We use **high-end mass analysers** alongside a variety of ionisation techniques to cover a broad range of samples and workflows. Set within the Science & Technology team, we combine MS readouts with other biomarker platforms, advanced automation, acoustic liquid handling, complex cell culture or *in vivo* imaging.

We specialise in:

- High-throughput MS methods
- Advanced MS imaging
- Isotope tracing experiments
- Custom assay development
- In-depth analysis of drug response
- Technology development & testing

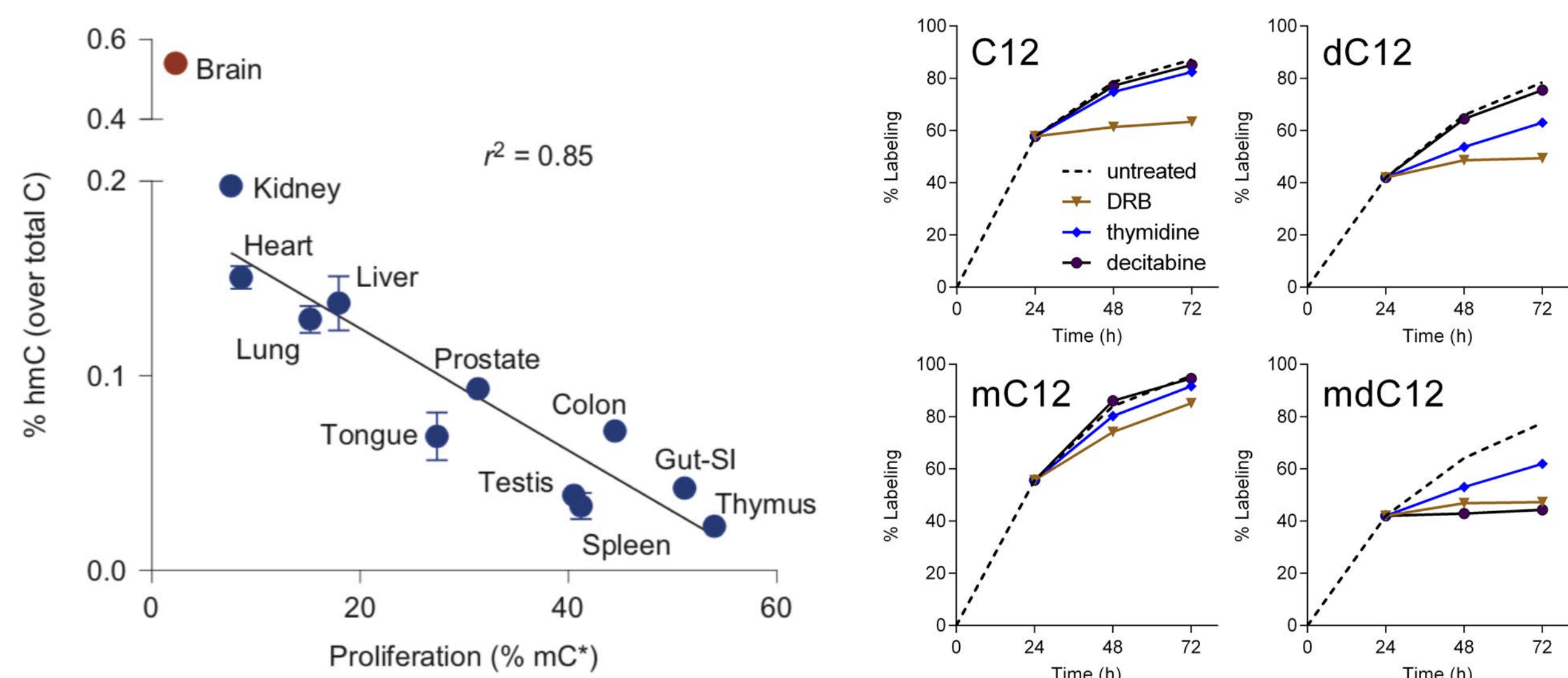
Our growing capability includes:

- Xevo G2-XS, TQ-XS and Synapt G2-Si
- ESI, nanoESI, DESI and REIMS sources
- I-Class and M-Class LC systems
- Echo555 acoustic liquid handlers
- HighRes robotic arm
- Progenesis QI & Genedata Expressionist

EXAMPLE WORKFLOW FOR THE ANALYSIS OF NUCLEIC ACIDS

▪ **Experimental design.** A non-toxic, isotopically labelled probe $^{13}\text{C}_9,^{15}\text{N}_3$ -cytidine is administered to cells or animals, tagging nascent genomic DNA and RNA, followed by a treatment with a studied compound. DNA & RNA are co-purified, subjected to enzymatic lysis to nucleosides and analysed by a targeted HPLC-MS/MS method.

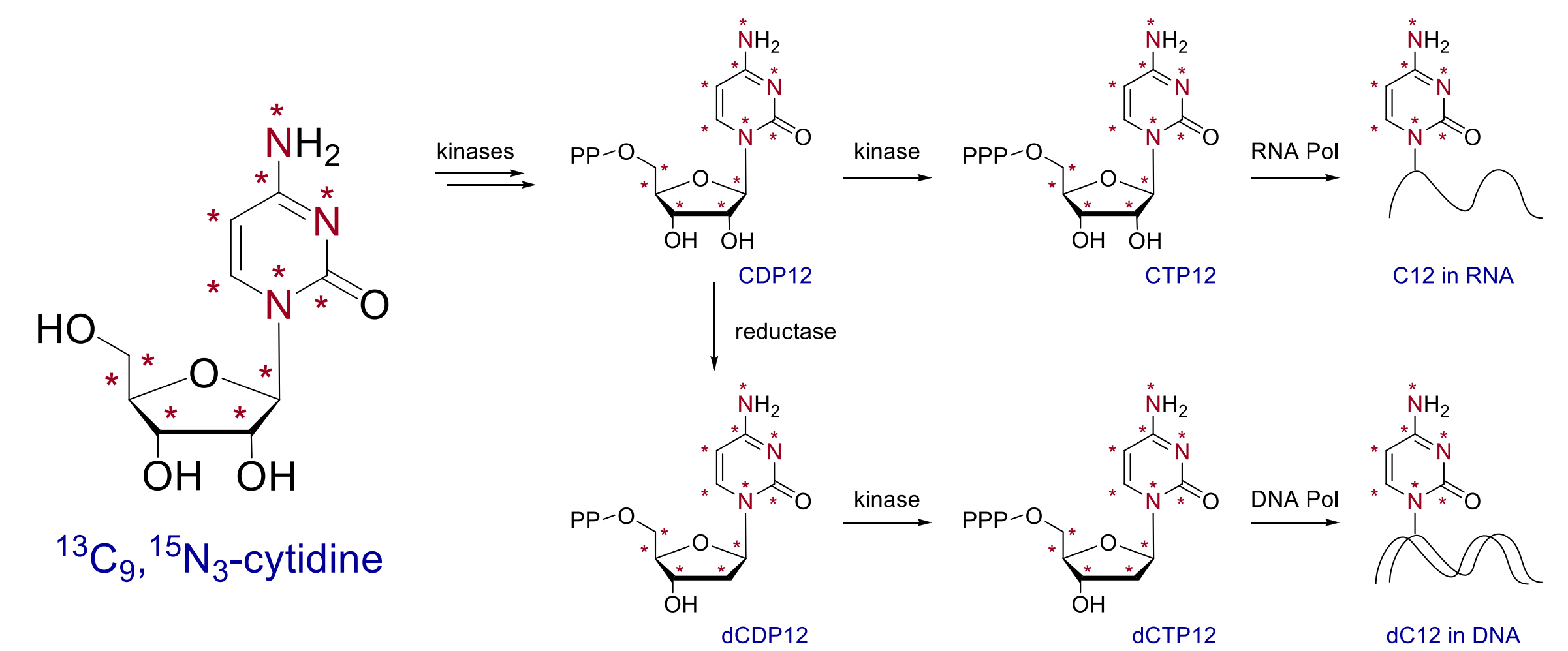
- **What do we measure?** Levels of labelled and unlabelled cytosine variants in DNA and RNA, guanine and oxidised guanine in DNA. Custom modifications can be added to the list.



▪ **What information can be obtained?** We can accurately quantify changes in proliferation and transcription rates, cytosine methylation and oxidation, presence of DNA damage markers due to treatment or genetic manipulation. Incorporation of unnatural nucleosides into RNA and genomic DNA can be investigated.

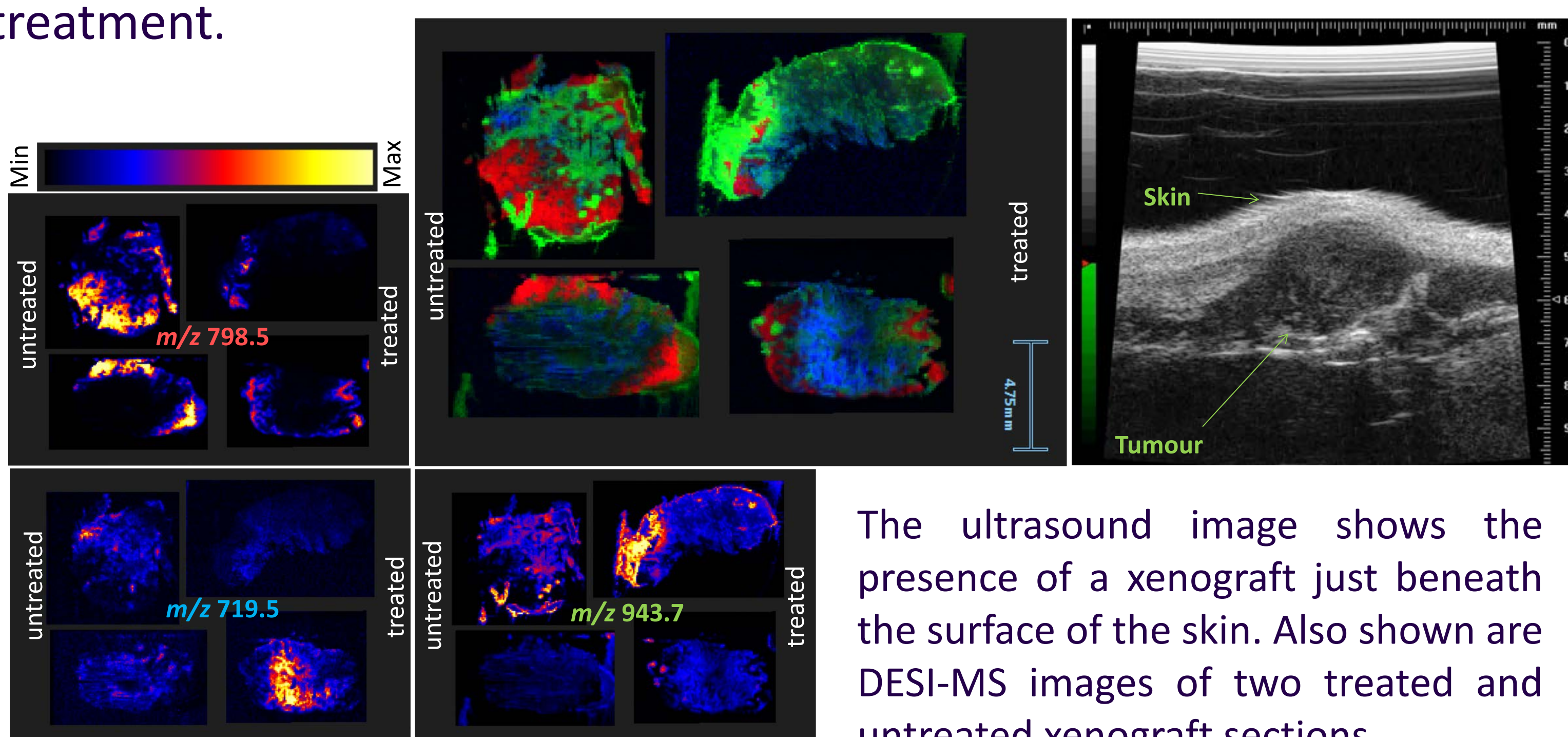
- **Who will benefit?** Companies and organisations developing oligonucleotide therapeutics, compounds against epigenetic targets, biomarkers based on modified nucleic acids, methods for targeted delivery of cytotoxic drugs and others.

Bachman, *et al.*, *Nature Chemistry* 6, 1049-55 (2014) and unpublished data



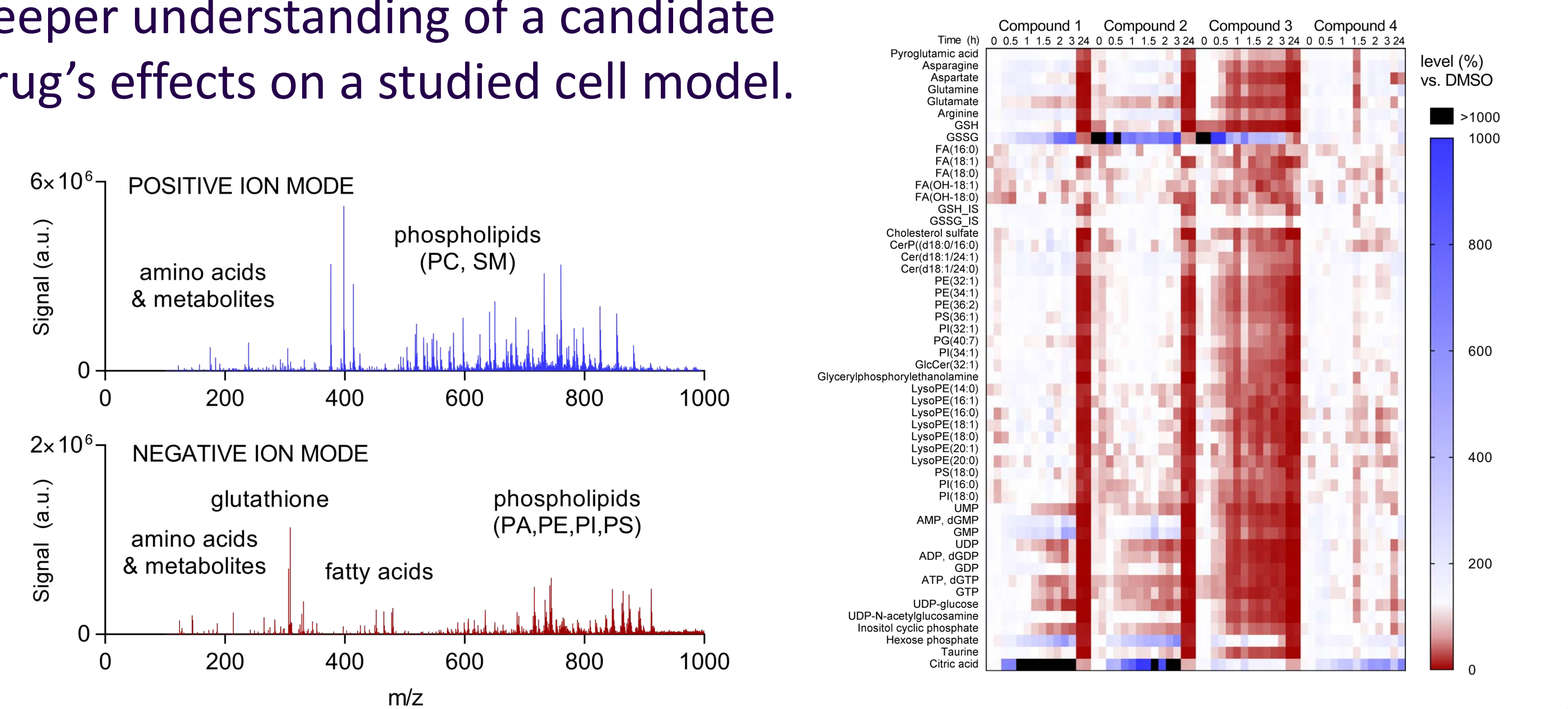
EXAMPLE DESI-MS IMAGING DATA

As part of a project aiming to help commercialise a novel method for targeted drug delivery, we analysed xenografts from CD1 mice by DESI-MS imaging. We compare specific regions via multivariate analysis to reveal differences in small molecule expression resulting from drug treatment.



HIGH-THROUGHPUT MS

We are developing a variety of direct infusion ("shotgun") workflows for rapid high-content analysis of cultured cells and other biological samples such as blood plasma. Increasing the throughput opens new possibilities such as powerful time-course experiments leading to a deeper understanding of a candidate drug's effects on a studied cell model.

Sinclair, Bachman, *et al.*, submitted