



METABOLOMICS RESEARCH

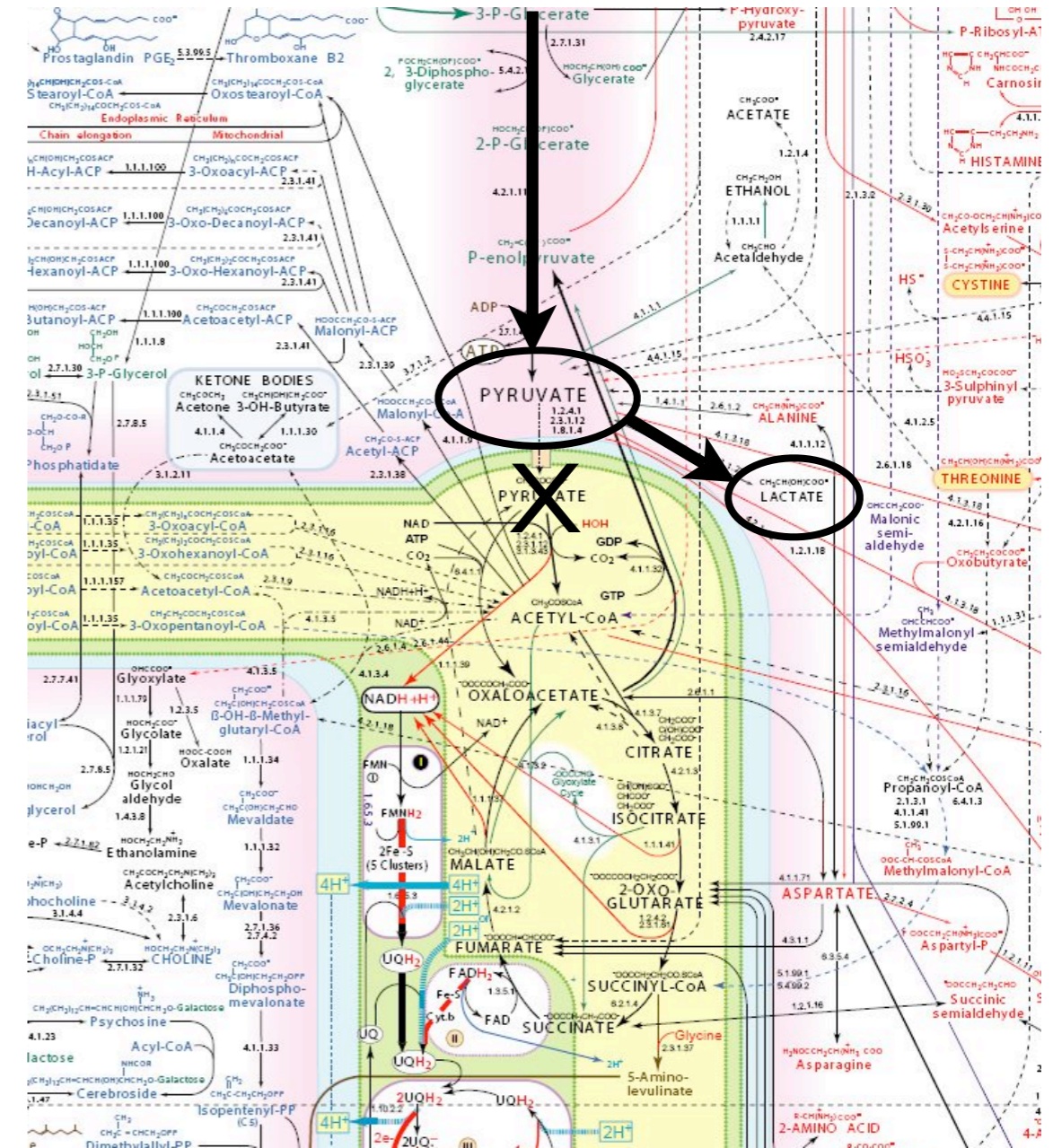
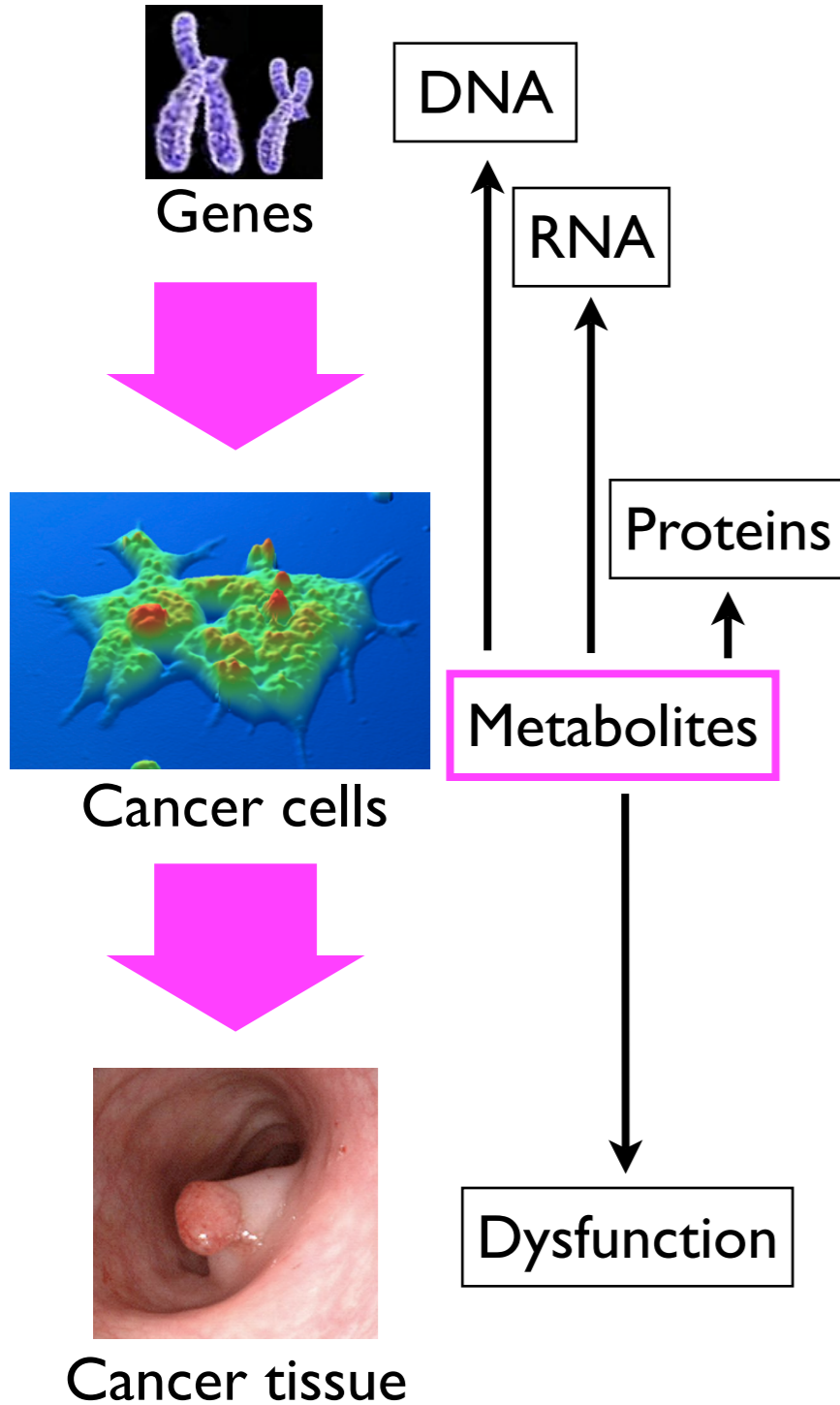
CARMeN project



METABOLOMICS

Fundamental, clinical & pre-clinical research

Metabolomics research



METABOLOMICS

Fundamental, clinical & pre-clinical research

Metabolomics for cancer research

University Hospitals of Strasbourg (I.J. Namer, J.P. Bellocq)

University of Strasbourg / CNRS (K. Elbayed)

Bruker France (M. Piotto)

Regional Cancer Institute

CARMeN project

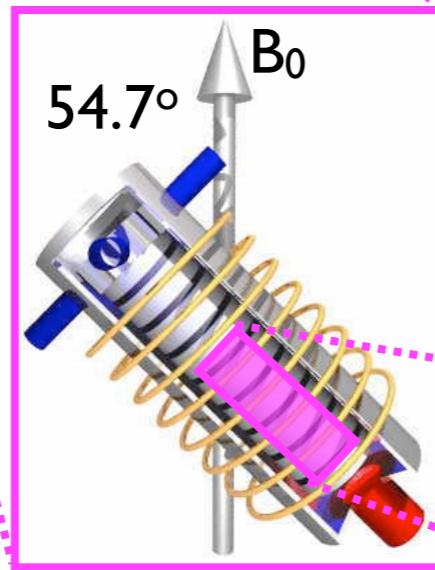
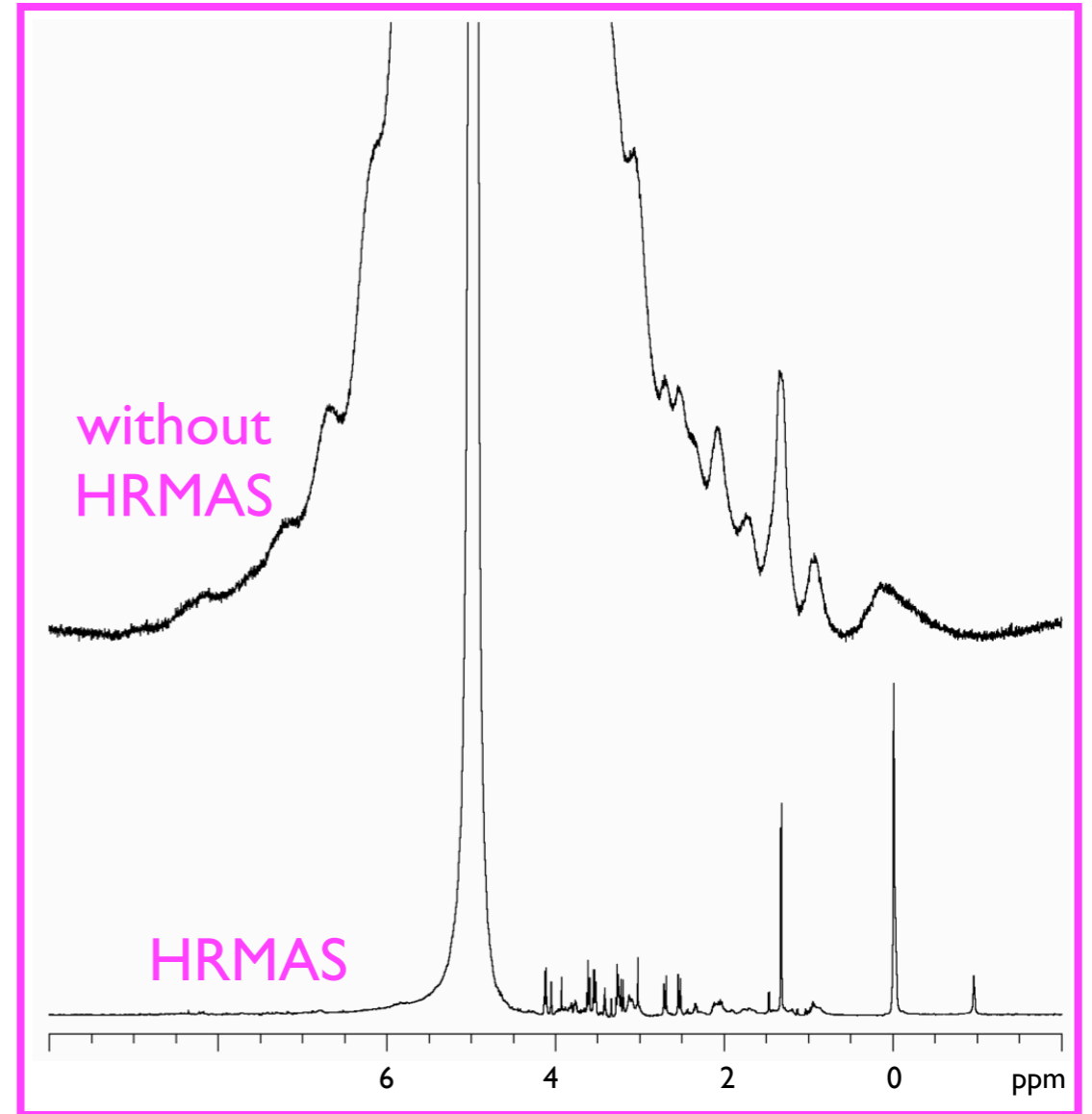
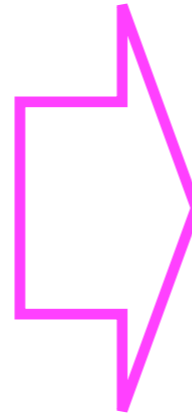
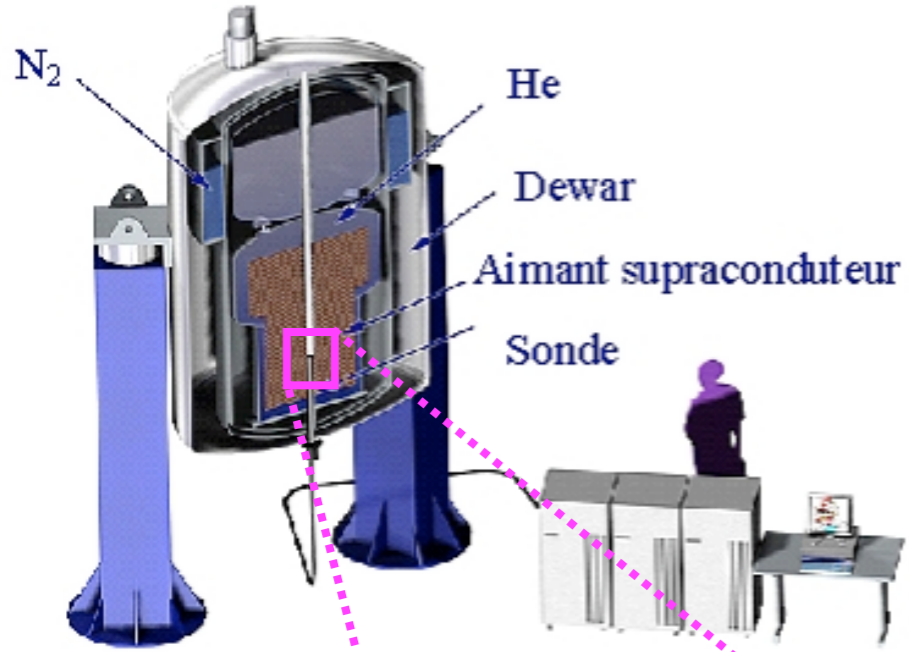
2.7 millions €



Strasbourg's Hautepierre Hospital
11.7 T HRMAS-NMR System

METABOLOMICS

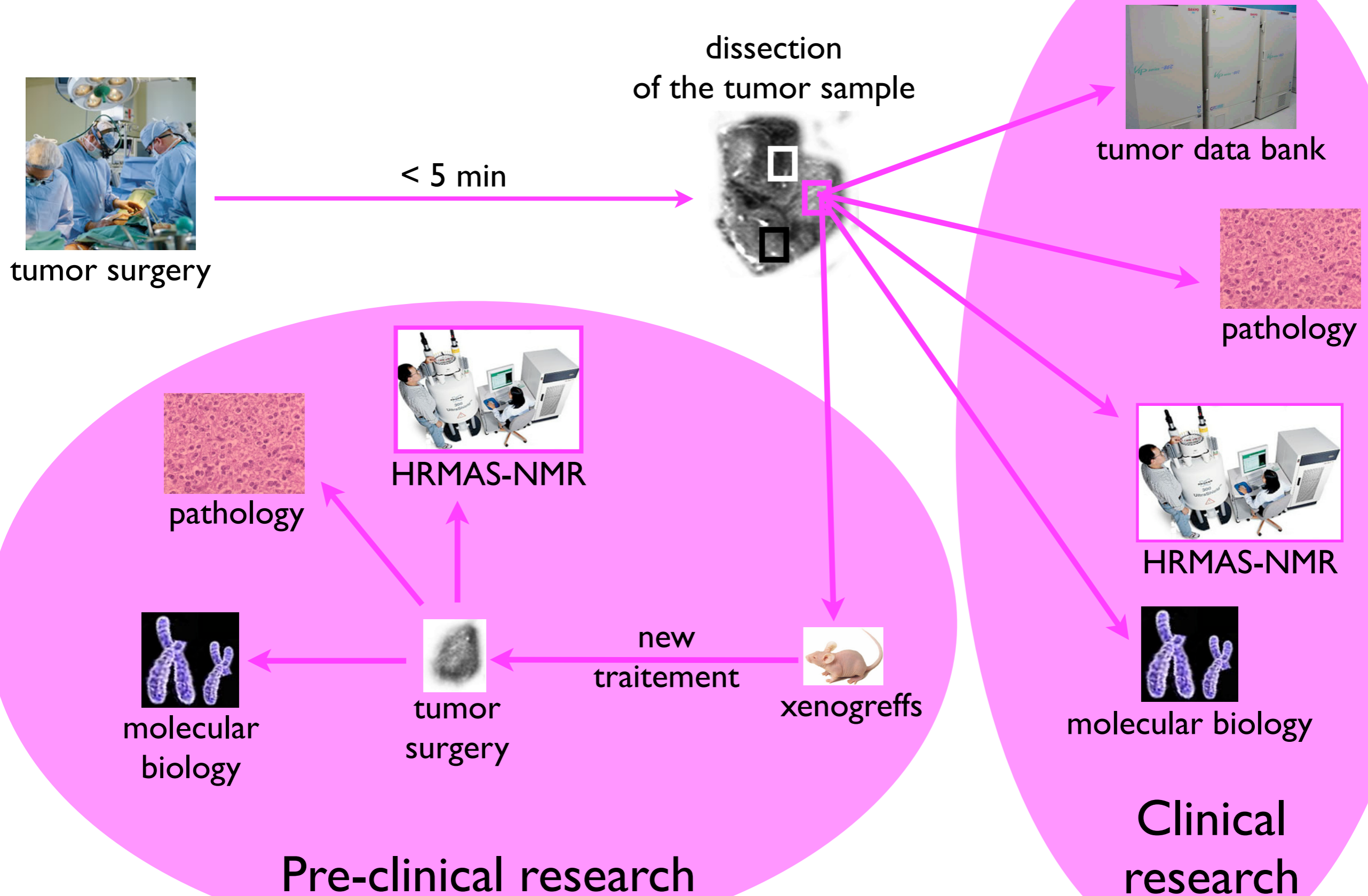
Fundamental, clinical & pre-clinical research



biological tissue
(1-20 mg)

METABOLOMICS

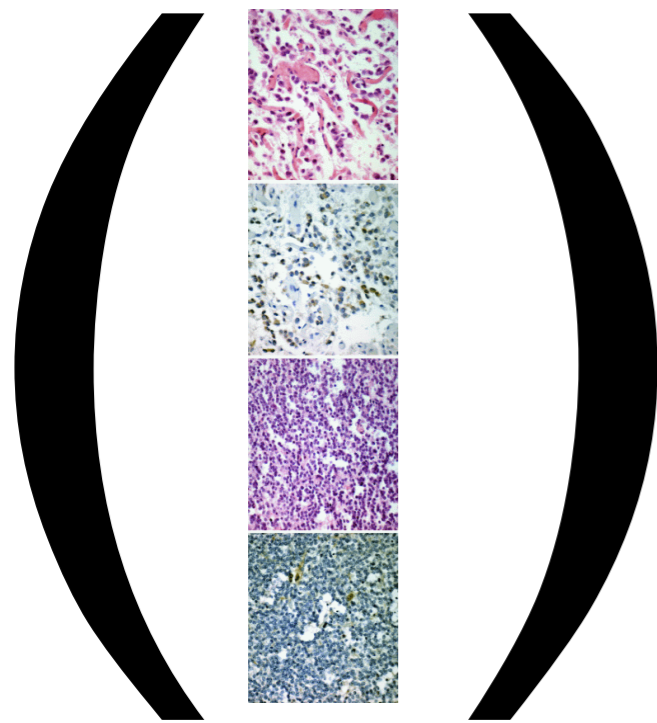
Fundamental, clinical & pre-clinical research



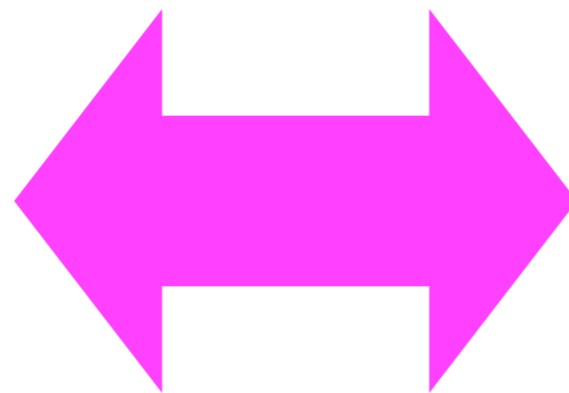
METABOLOMICS

Fundamental, clinical & pre-clinical research

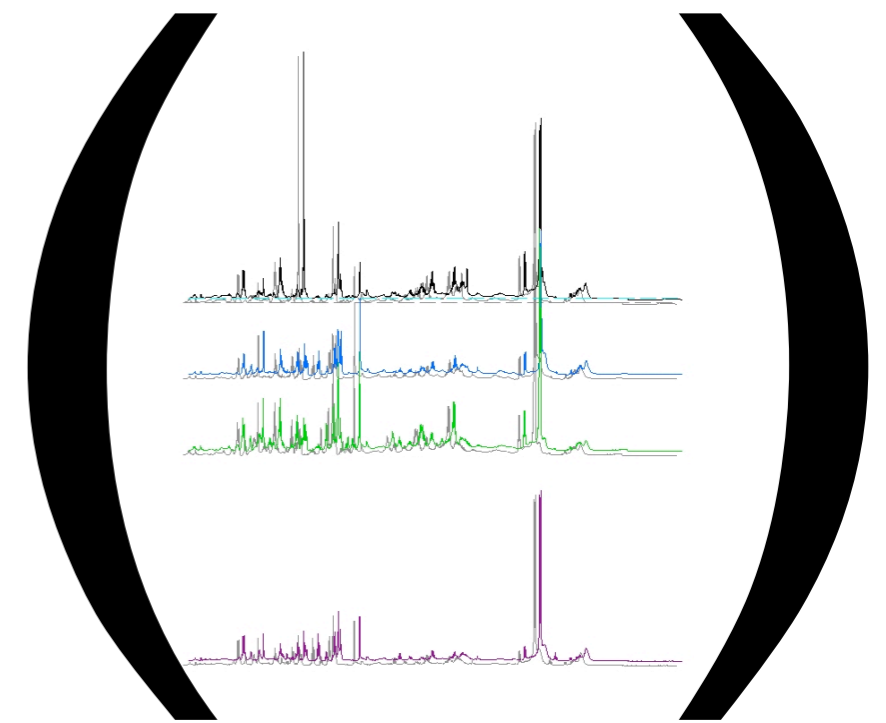
NMR Metabolomics database in cancerology



Histopathology, molecular biology,
prognosis, medical imaging...



Statistical models
(PCA, PLS-DA)

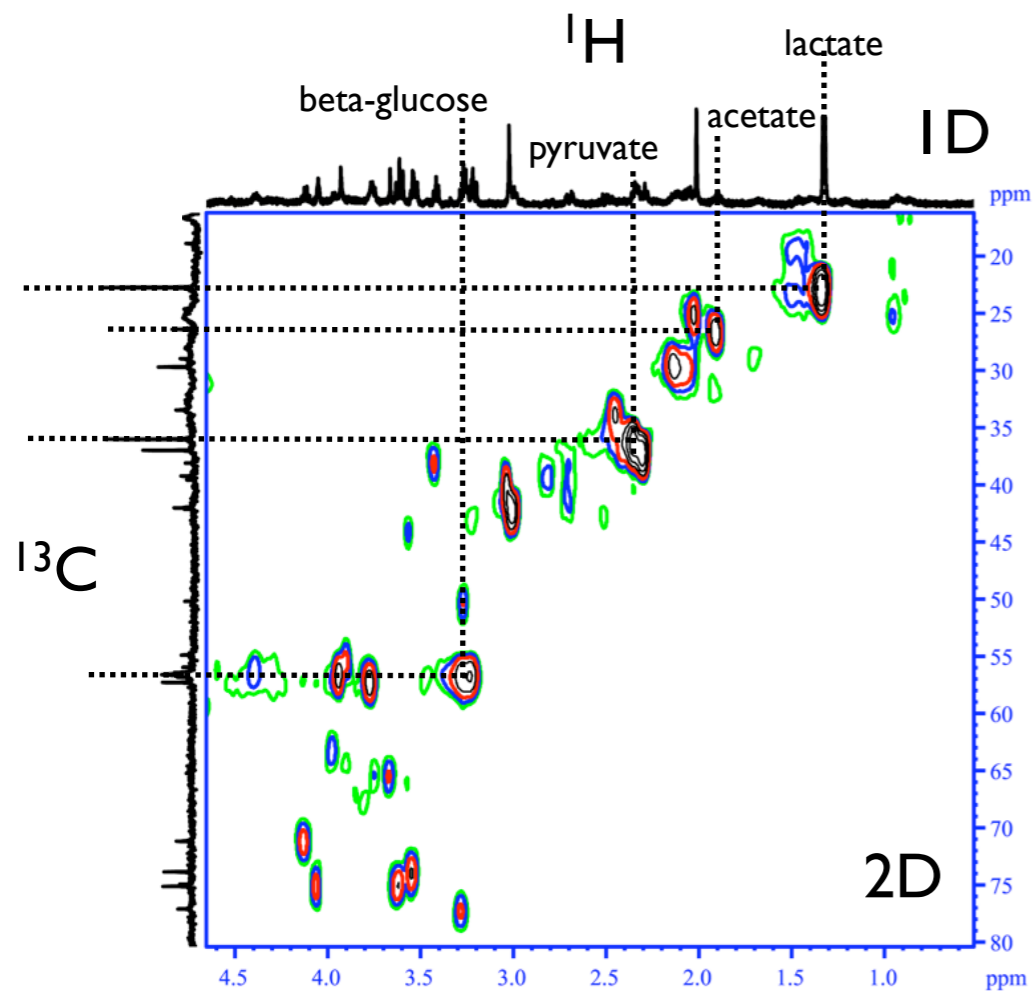


Metabolomics data

METABOLOMICS

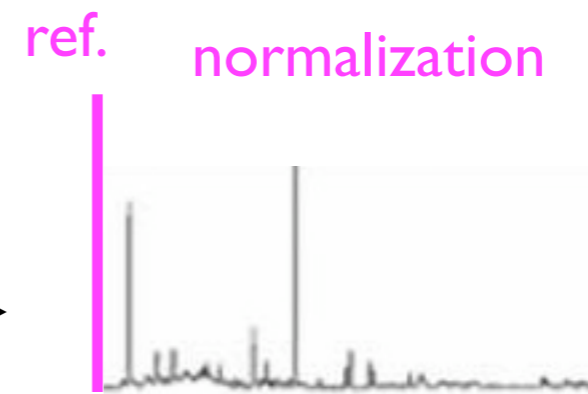
Fundamental, clinical & pre-clinical research

HRMAS-NMR
spectroscopy



resolution : 10 microM

Pretreatment of 1D spectra



sampling



Statistical treatment

PCA, PLS-DA

METABOLOMICS

Fundamental, clinical & pre-clinical research

Publications:

G Erb, K Elbayed, M Piotto, J Raya, A Neuville, M Mohr, D Maitrot, P Kehrli, IJ Namer : Towards improved grading of malignancy in oligodendrogliomas using metabolomics. *Magnetic Resonance in Medicine* 59: 959-965, 2008.

M Piotto, FM Moussallieh, B Dillmann, A Imperiale, A Neuville, C Brigand, JP Bellocq, K Elbayed, IJ Namer : Metabolomic characterization of primary human colorectal cancers using high resolution magic angle spinning ¹H magnetic resonance spectroscopy. *Metabolomics* 5: 292-301, 2009.

A Imperiale, K Elbayed, FM Moussallieh, A Neuville, M Piotto, JP Bellocq, P Lutz, IJ Namer : Metabolomic pattern of childhood neuroblastoma obtained by ¹H high resolution magic angle spinning (HRMAS) NMR spectroscopy. *Pediatric Blood & Cancer* (in press), 2010.

J Detour, K Elbayed, M Piotto, FM Moussallieh, A Nehlig, IJ Namer : Ultra fast in vivo microwave irradiation for enhanced metabolic stability of brain biopsy samples during HRMAS NMR analysis. *Journal of Neurochemistry* (submitted), 2010.

N Daci-Youcef, S Froeliech, FM Moussallieh, S Heikkinen, D Dembele, B Lhermitte, K Elbayed, C Koehl, IJ Namer, J Auwerx : Gene expression mapping of HDACs and co-factors correlates with metabolomic profile and helps to identify human brain tumor subgroup signatures. In preparation for *Cancer Research*, 2010.

D Ben Sellem, K Elbayed, A Neuville, FM Moussallieh, M Piotto, JP Bellocq, IJ Namer : Metabolomic approach to ovarian cancers: HRMAS NMR investigation. In preparation for *Gynecologic Oncology*, 2010.

K Elbayed, FM Moussallieh, A Neuville, H Lang, M Piotto, JP Bellocq, IJ Namer : Metabolomic approach to renal cancers: HRMAS NMR investigation. In preparation for *NMR in Biomedicine*, 2010.

The French connection

Meanwhile, a second team in Strasbourg is hoping to use its own NMR machine, which was installed in Hautepierre hospital in 2007, to analyse colon and kidney samples. Starting next year, the machine will provide surgeons with information about whether they have successfully removed cancers from patients while they are on the operating table.

"We're confident we've been able to find decent biomarkers for kidney and colon biopsies," says Martial Piotto, head of the NMR application laboratory of scientific instrument maker Bruker BioSpin in Wissembourg, France, which made the Hautepierre NMR machine. "What we'd like to do now is perform some real-time analysis during a surgical operation."

Piotto, together with Izzie Namer of the nuclear medicine department at the University Hospitals of Strasbourg and Karim Elbayed, an NMR spectroscopist at the University of Strasbourg, have already built databases containing metabolic profiles of healthy and cancerous tissue from many different organs. They now plan to spend the next two–three months looking at whole diseased colons and kidneys excised from patients to see whether they can accurately identify cancerous growths from the concentrations of different metabolites in cells. By June 2010, they hope to use their expertise to inform surgical decisions.

Published online 14 December 2009 | Nature |
doi:10.1038/news.2009.1128

News

Surgeons get real-time tissue profiling

Nuclear magnetic resonance technology could reduce time spent under the knife.

Ananyo Bhattacharya

Chemical fingerprints of tissue samples taken during operations could soon help surgeons to decide where to make their incisions. Two groups — one based in the United Kingdom, the other in France — are leading efforts to use nuclear magnetic resonance (NMR) spectroscopy to analyse the metabolites in biopsies. The analyses should reveal whether cells in the sample are healthy and — for the first time — relay that information back to the operating theatre within minutes.

In February, a team led by Jeremy Nicholson, head of the department of surgery and cancer at Imperial College London, is planning to install a £300,000 (US\$490,000) NMR machine that can study solid samples at a surgical unit at St Mary's Hospital. It is the first step in a programme that could later see the instruments rolled out to intensive-care units and other wards in hospitals affiliated with Imperial.



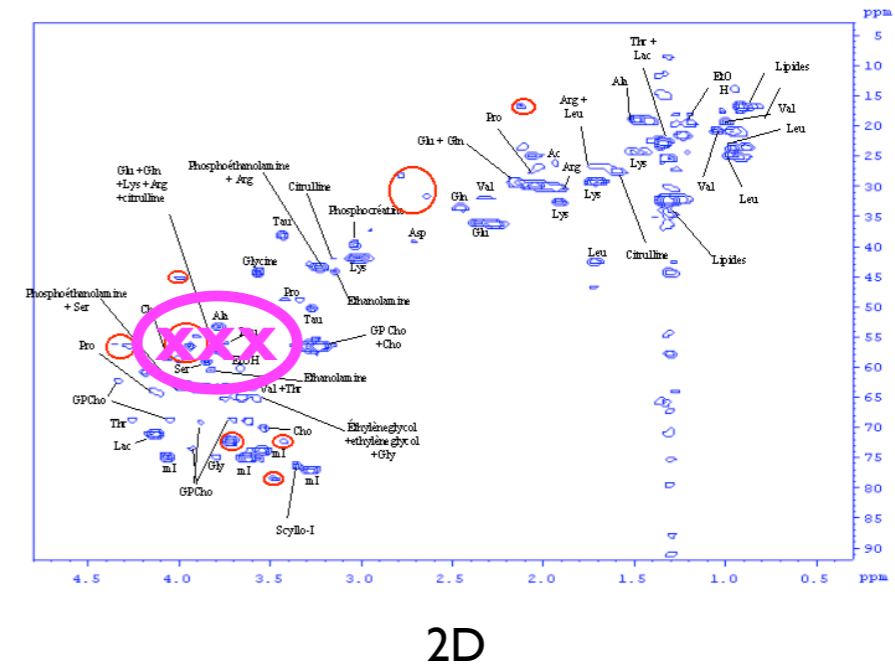
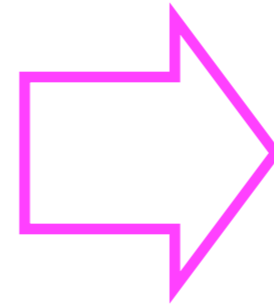
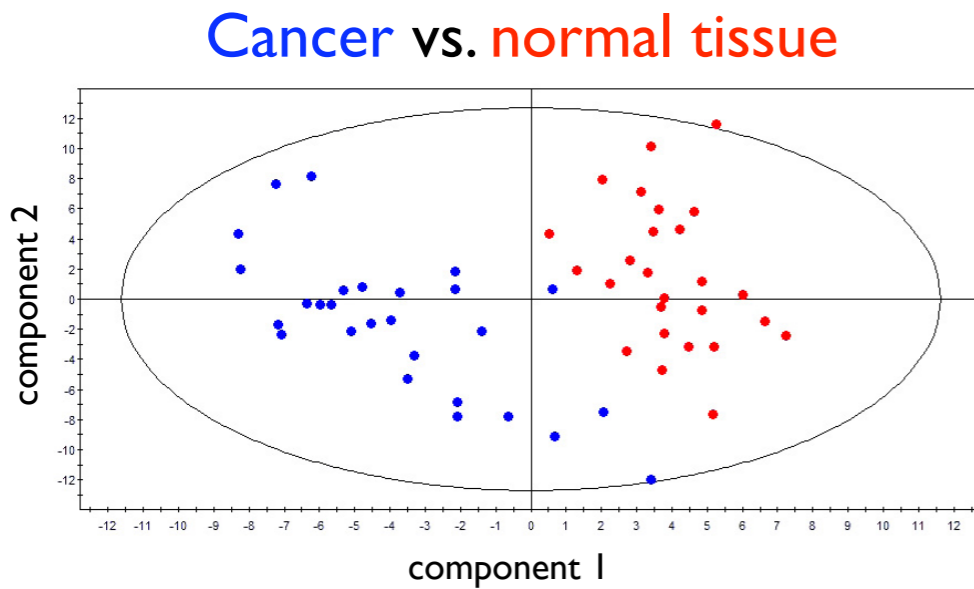
Could tomorrow's surgeons be guided by nuclear magnetic resonance?

R. McVay/Getty

METABOLOMICS

Fundamental, clinical & pre-clinical research

Metabolomic identification of biomarkers



Production of the $[^{13}\text{C}_2]$ -XXX

AlsaChim

single i.v. injection of 20 mM $[^{13}\text{C}_2]$ -XXX



tumor resection



HRMAS (^1H - ^{13}C)

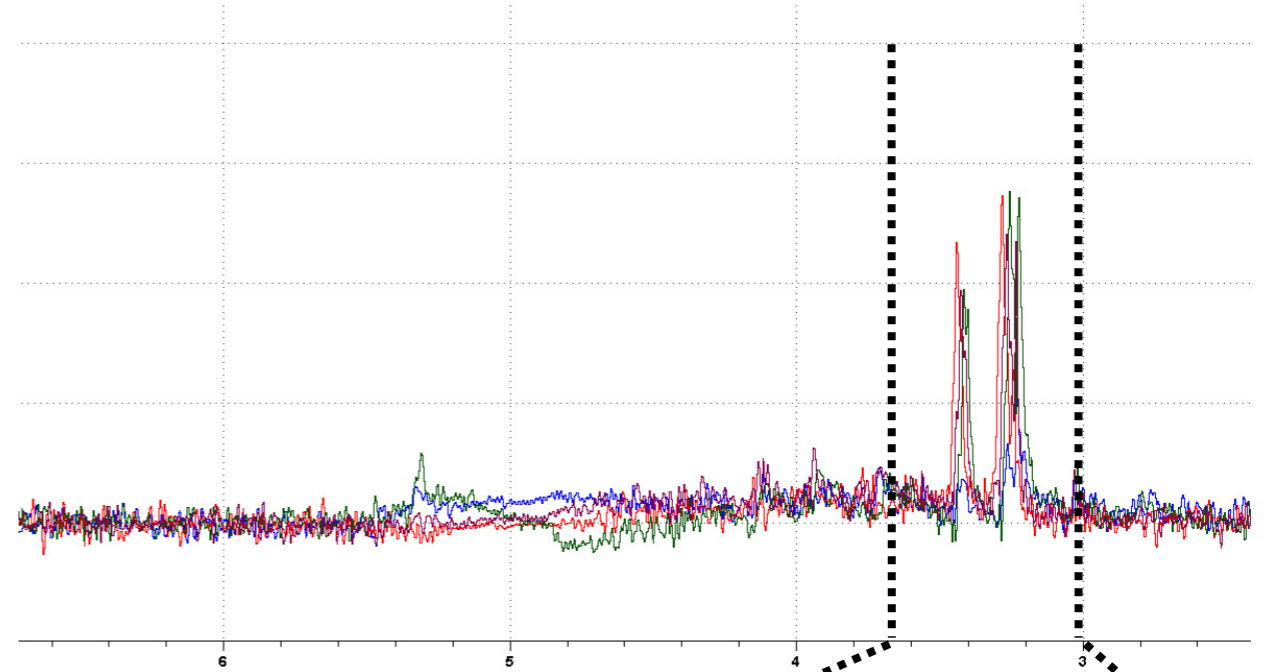
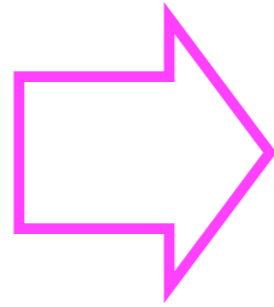
Experimental nude mouse model of human cancer

METABOLOMICS

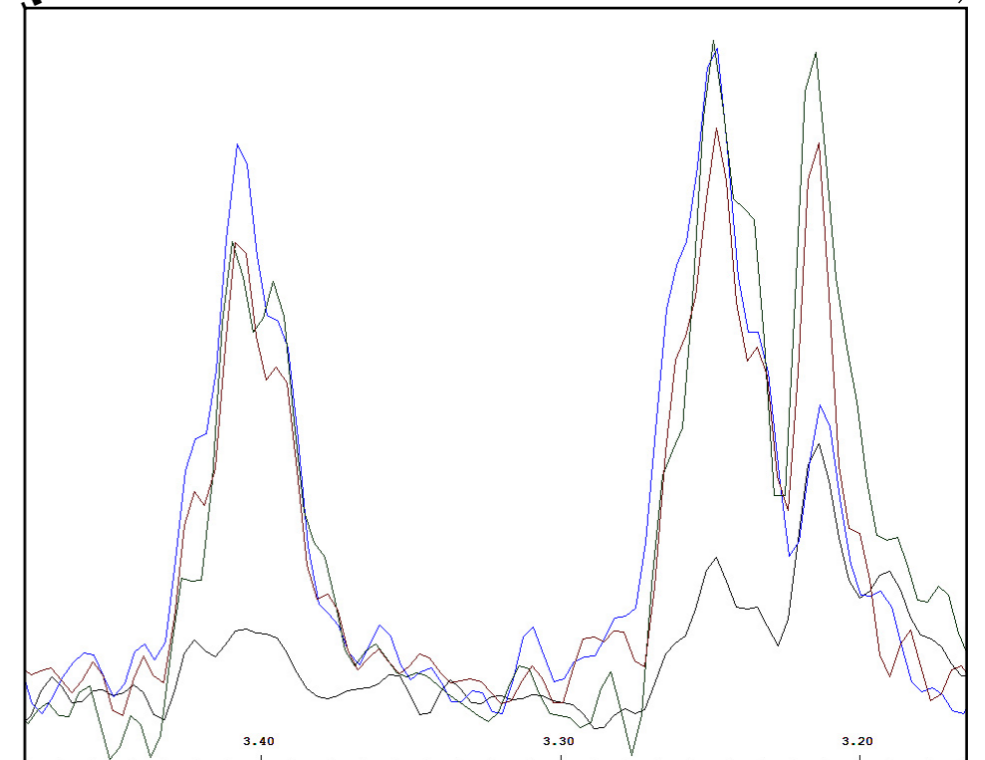
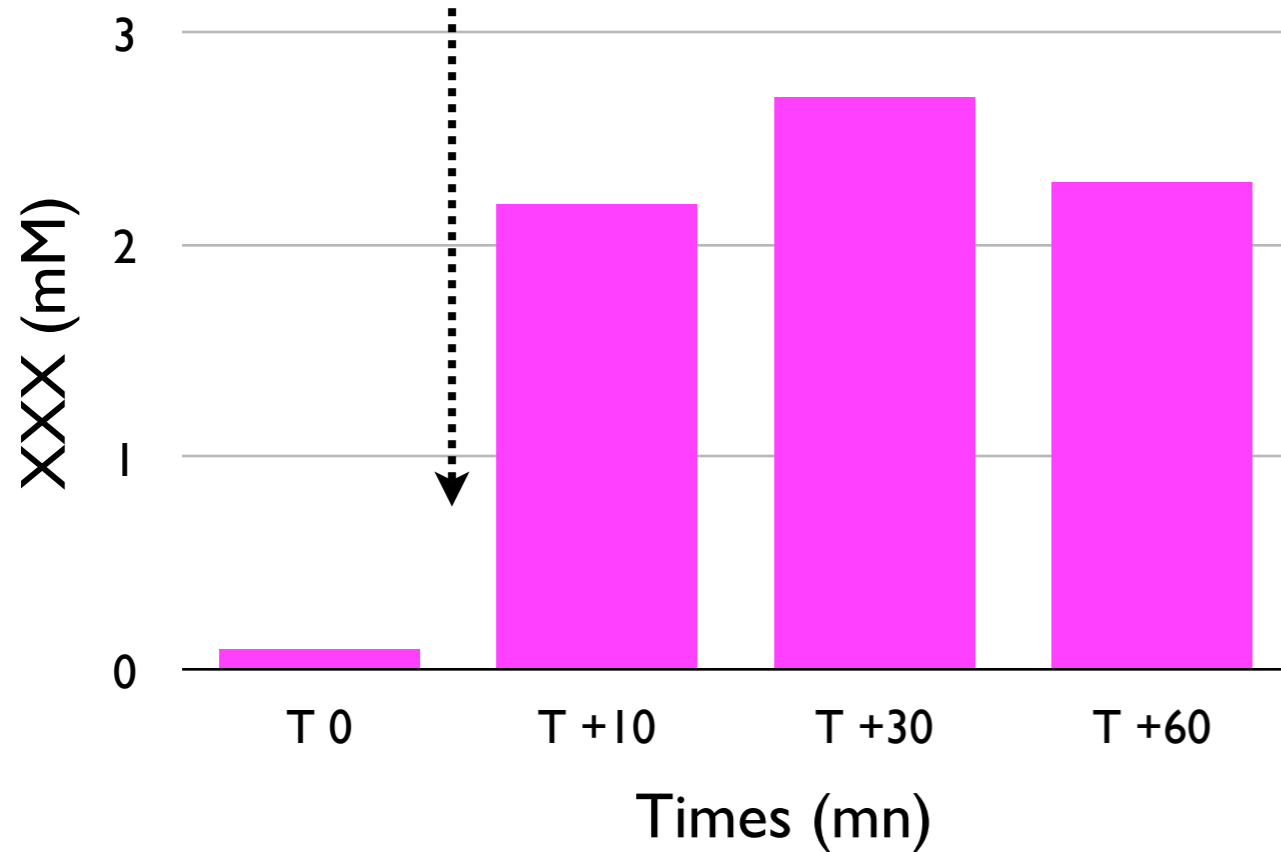
Fundamental, clinical & pre-clinical research



HRMAS (^1H - ^{13}C)



single i.v. injection of
20 mM [$^{13}\text{C}_2$]-XXX

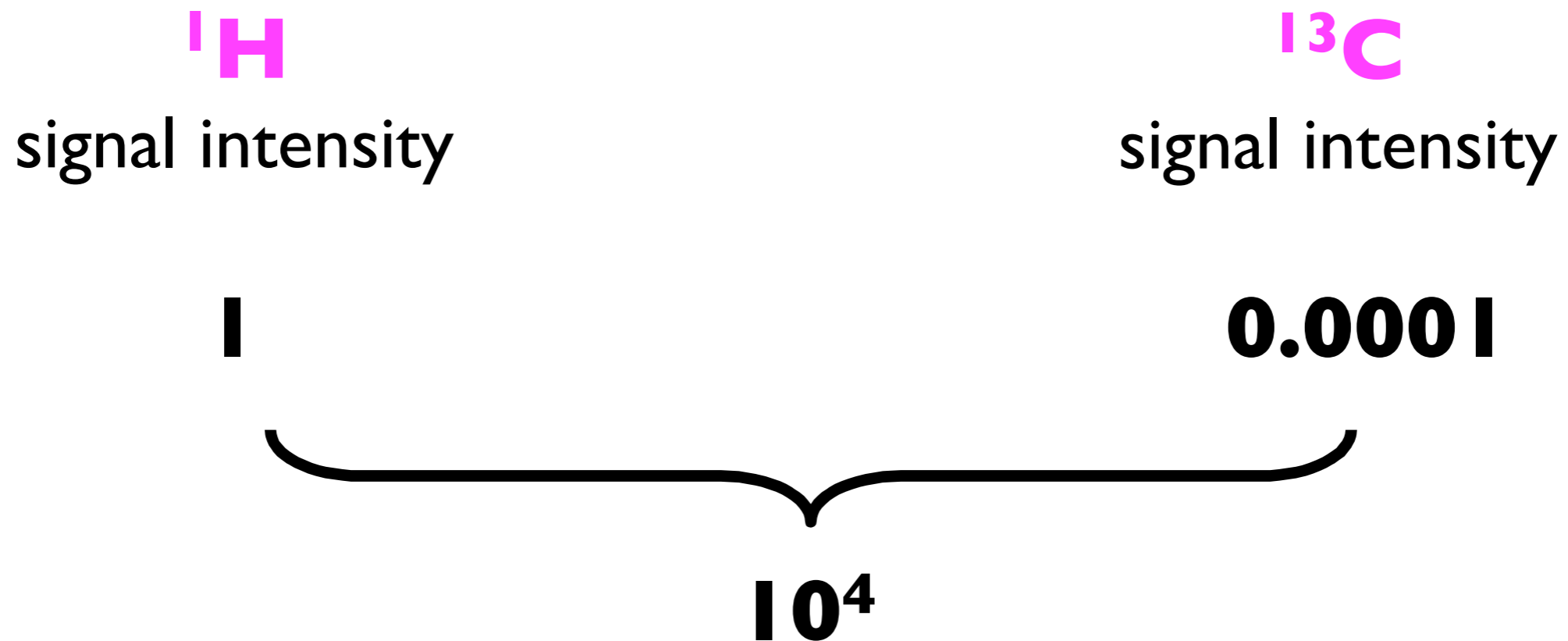


METABOLOMICS

Fundamental, clinical & pre-clinical research

CARMeN *in vivo*: ^{13}C -NMR metabolic imaging *in vivo*

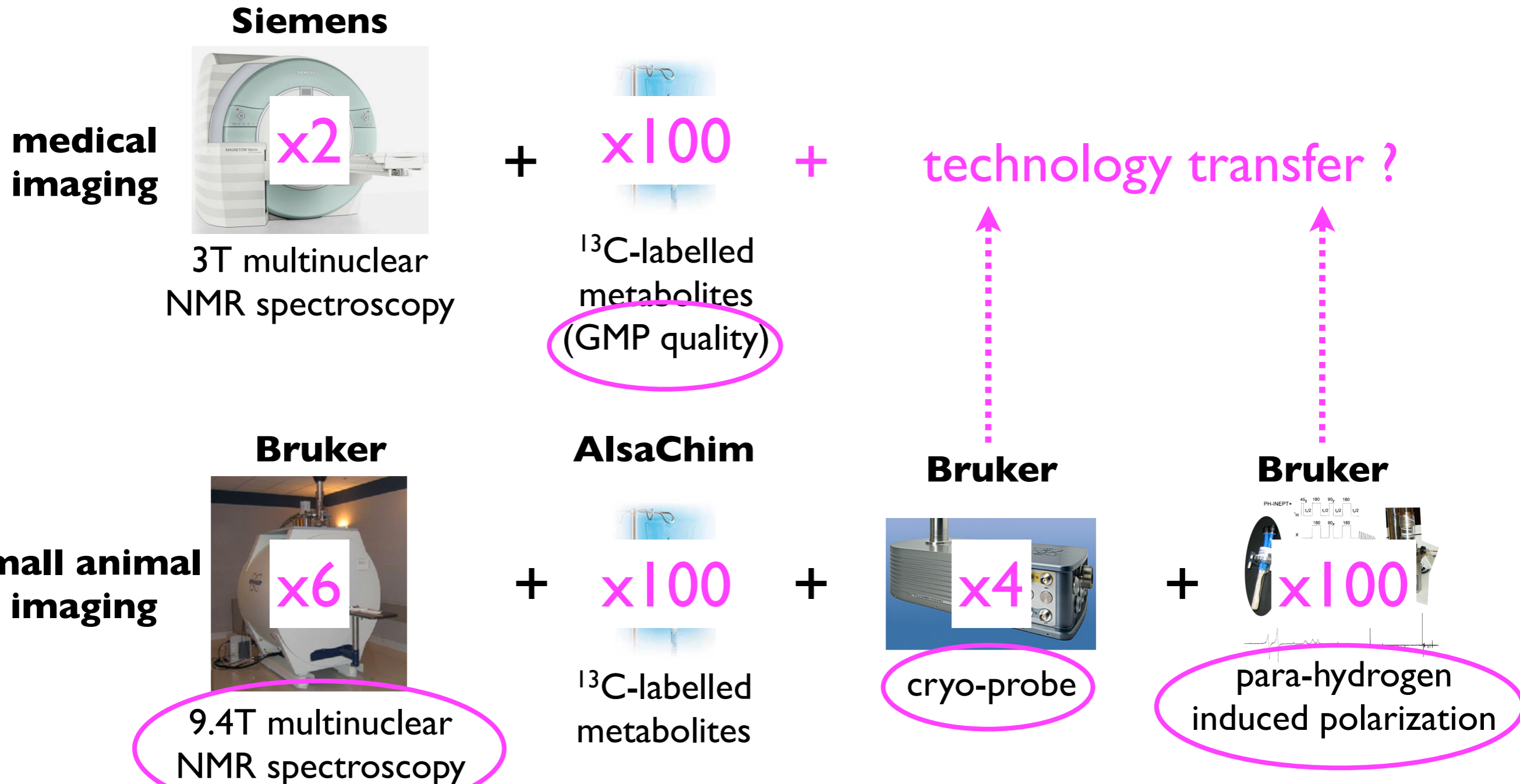
Major problem : **sensitivity**



METABOLOMICS

Perspectives

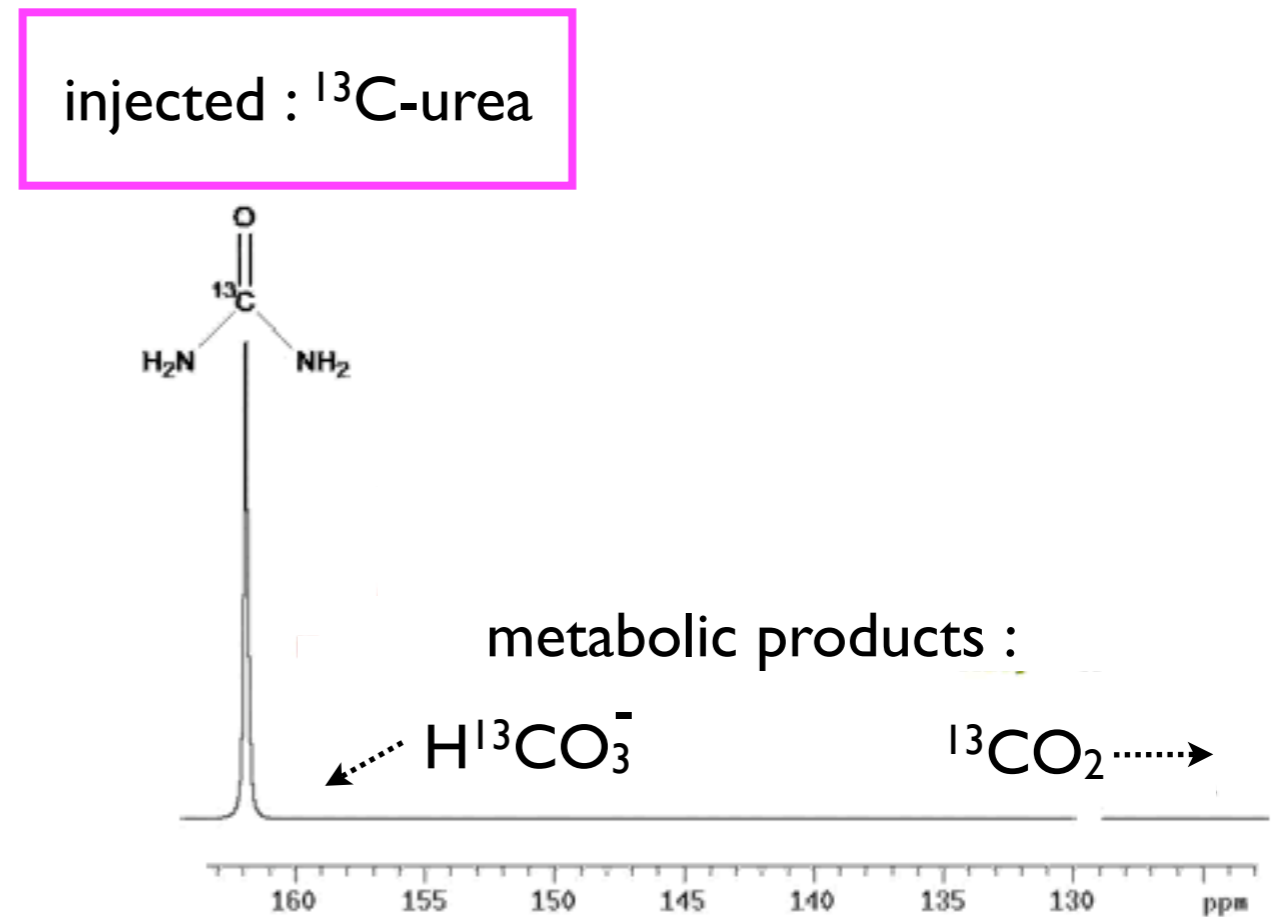
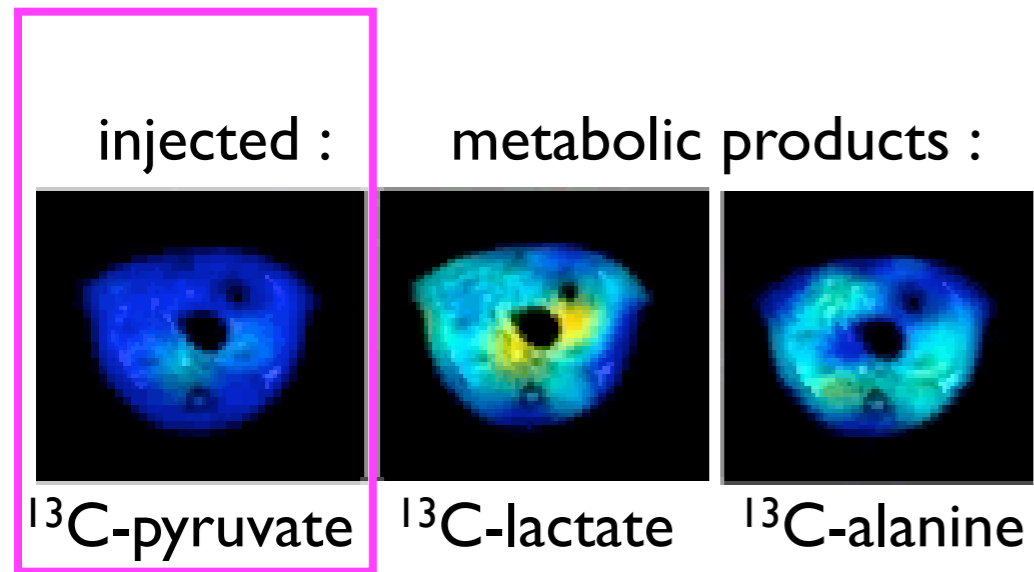
CARMeN *in vivo*: ^{13}C -NMR metabolic imaging *in vivo*



METABOLOMICS

Perspectives

Real time metabolic imaging *in vivo*





Thanks for your attention