METABOLOMICS RESEARCH

CARMen project
Metabolomics research

DNA

RNA

Proteins

Genes

Metabolites

Cancer cells

Dysfunction

Cancer tissue
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
METABOLICOMICS

Fundamental, clinical & pre-clinical research

- Biological tissue (1-20 mg)

- Without HRMAS
- HRMAS
METABOLOMICS

Fundamental, clinical & pre-clinical research

tumor surgery
< 5 min
HRMAS-NMR
pathology
tumor data bank
molecular biology
xenogreffs
new traitement
molecular biology
Clinical research
Pre-clinical research

dissection of the tumor sample
Histopathology, molecular biology, prognosis, medical imaging...

NMR Metabolomics database in cancerology

Statistical models (PCA, PLS-DA)

Metabolomics data
HRMAS-NMR spectroscopy

1^3C

1^H

Beta-glucose, pyruvate, acetate, lactate

Resolution: 10 microM

Pretreatment of 1D spectra

Normalization

Sampling

Statistical treatment

PCA, PLS-DA

METABOLIC MAPPING

Fundamental, clinical & pre-clinical research
Publications:


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 Pietto, 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."

Pietto, 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

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.
Metabolomic identification of biomarkers

Cancer vs. normal tissue

Production of the $^{13}$C$_2$-XXX

AlsaChim

Single i.v. injection of 20 mM $^{13}$C$_2$-XXX

Experimental nude mouse model of human cancer

Tumor resection

HRMAS ($^1$H-$^{13}$C)
HRMAS (\textsuperscript{1}H-\textsuperscript{13}C)

Single i.v. injection of 20 mM \([\textsuperscript{13}C_2]\)-XXX

XXX (mM)

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METABOLOMICS
Fundamental, clinical & pre-clinical research

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

Major problem: *sensitivity*

$^1$H signal intensity

$^{13}$C signal intensity

$1$ $\times 10^4$

$0.0001$
**METABOLOMICS Perspectives**

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

- Siemens medical imaging: 3T multinuclear NMR spectroscopy ($\times 2$)
- Bruker small animal imaging: 9.4T multinuclear NMR spectroscopy ($\times 6$)
- AlsaChim: $^{13}$C-labelled metabolites (GMP quality) ($\times 100$)
- Bruker cryo-probe ($\times 4$)
- Bruker para-hydrogen induced polarization ($\times 100$)

Technology transfer?
Real time metabolic imaging *in vivo*

Injected: $^{13}$C-urea

Metabolic products:
- $^{13}$C-pyruvate
- $^{13}$C-lactate
- $^{13}$C-alanine

Metabolic products:
- $^{13}$CO$_2$
- $^{13}$CO$_3^-$

http://www.imagnia.se
Thanks for your attention