METABONOMICS-based RESEARCH
at UMONS

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MBX Joint Meeting – Ghent – September 29th 2017
School of Medicine and Pharmacy

Department of Human Biology & Toxicology

http://portail.umons.ac.be/FR/universite/facultes/fmp/services/toxico/Pages/default.aspx
NMR background at UMONS

Since 1980, laboratory of Organic Chemistry

Research

Interest in the development of Contrast Agent for MRI

⇒ Relaxometry & MRI

⇒ Profs. Robert Muller and L. Vander Elst
NMR-based Metabonomics background at UMONS

• From 2000 - 2005 COMET (Consortium of MBX in Toxicology)

• Initiated by J. Nicholson’s team

• Including Imperial College and 6 Pharmaceutical companies
Candidate molecules
Consortium on Metabonomic in Toxicology

Imperial College-London
BMS  Lilly  Novo  Pfizer  Pharmacia  Roche

150 prototoxicants
Acute dosing
$^1$H-NMR analysis
Database + Chemometrics models for toxicity prediction

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COMET: Control Model

Identifying abnormal urine samples

- 4521 “normal” urine samples
- PCA-based approach
- Determine the distance to the model (DmodXPS+) as well as the probability of belonging to the model (PmodXPS+):

Test sample

- Normal
- Marginal: 95%<x< 99%
- Abnormal: <95%

Prediction and Classification of Drug Toxicity Using Probabilistic Modeling of Temporal Metabolic Data: The Consortium on Metabonomic Toxicology Screening Approach
T. Ebbels, H. Keun, O. Beckonert, M. Bollard, J. Lindon, E. Holmes, and Jeremy K. Nicholson
Journal of Proteome Research/2007
COMET: CLOUDS Model
(Classification Of Unknowns by Density Superposition)

Identifying toxicity type

- PNN-based model (Probabilistic Neural Network – Specht 1990)

Cardiac toxicity

Renal toxicity

Liver toxicity

Test sample
Develop & Apply tools in Predictive Toxicology including:

- QSAR models
- Cell cultures
- in vivo studies in rodents and invertebrates
- METABONOMICS
Experimental Protocol

Potential biomarkers

Pattern recognition

Potential biomarkers

1H NMR or MS

Urine

Blood

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In collaboration with the Chemistry Dpt (Prof. Sophie Laurent & Dr. Céline Hénoumont)
Initial research interest in the group:

- Metabonomics signatures of drug-induced adverse effects
- Liver, Kidney and cardiac toxicities
- Special focus on mitochondria
Sarcosine, mediator of trophoblast differentiation. From its discovery through an in vivo metabonomic approach to its validation in a trophoblastic stem cell model.
Evaluation of perturbations of mitochondrial biochemical pathways by metabonomic approach
Hypertension and hypothyroidism as potential biomarkers of the efficacy of Sunitinib, a tyrosine kinase inhibitor
Contribution of an integrated approach combining metabonomics and proteomics in the characterization and prediction of the toxic effects of xenobiotics. Application to the particular case of acetaminophen (APAP) and its meta isomer (AMAP)
IN 2012 NEW RESEARCH CENTER

UMHAP

UMONS Université de Mons

CHU AMBROISE PARÉ
From benchtop to bedside ....

To facilitate translational studies and better transpose lab results to clinics

ACCESS to phase I clinical studies
VINCENT RICHARD

BREAST CANCER

ONCOLOGY

Marilyn Duquesne

IMMUNOTHERAPY

KIDNEY CANCER
ATTRACTIVE RESEARCH ENVIRONMENT FOR INDUSTRIAL PARTNERS

PFIZER
METASUN
R. Conotte
PhD thesis

UCB Pharma
D. De Luca
PHD thesis

CARDIATIS
Sponsor of Dorian Maroil PhD thesis

DEXSIL
ACADEMIC PARTNERSHIPS

FNRS CONTACT GROUP
ULG : Profs. P. De Tullio, M. Frederich
UCL : Prof. B. Govaerts

CORENTIN SCHEPKENS
KUL
Prof. J. Swinnen
LIPIDOMICS
LYSOCAN (PhD thesis)
WALLONIA PUBLIC FUNDING

GREENWIN PROJECTS
MEMORIS
DUFERCO & SITEREM
+ academic partners

AUDE DEVALCKENEER

METABONOMICS in ECOTOXICOLOGY
OUR NEAR FUTURE ... 2018
EU FUNDING
BIOPROFILING UNIT

METAVISION
NMR-MS coupled for
MBX PROFILING

Call for tenders ongoing ........
METAVISION

ACADEMIC PROJECTS

OPEN to PRIVATE PARTNERS
UMHAP CLINICAL STUDIES

INDUSTRIAL PARTNERS

MBX LAB at UMONS

ACADEMIC PARTNERS (FNRS CONTACT GROUP)

YOU?

UMONS = 2017
THANK YOU!

VIRGINIE DELSINNE

ZEHRA KAHVECIOGLU
Winners of UMONS scholarships

MATTHIEU DALLONS

MANON DELCOURT

GOOD LUCK!
• Richard Vincent, Raphael. Conotte, David Mayne, Jean-Marie Colet. Does the 1H-NMR plasma metabolome reflect the host-tumor interactions in human breast; Oncotarget. 2017; 8:49915-49930

• Tagliatti Vanessa, Colet Jean-Marie, "Drug-Induced Impairment of Mitochondrial Fatty Acid Be- ta-Oxidation: A Metabonomic Evaluation in Rats" in HSOA Journal of Medical Genomics and Biomarkers, 3, 005 (2016)

• Duquesne Marilyn, Decleves Anne-Emilie, Deprez Eric, Nortier Joëlle, Colet Jean-Marie, "Interest of metabonomic approach in environmental nephrotoxicants : Application to aristolochic acid epoxidation" in Food & Chemical Toxicology (2017)


• Colet Jean-Marie, "Metabonomics in the Preclinical and Environmental Toxicity Field" in Drug Discovery Today, 13, 3-10, DDTEC428 (2015)

• Benourad Fouzia, Kahvecioglu ZEHRA CAGLA, Youcef-Benkada Mokhtar, Colet Jean-Marie, "Prospective evaluation of potential toxicity of repeated doses of Thymus vulgaris L. extracts in rats by means of clinical chemistry, histopathology and NMR-based metabonomic approach" in Drug Testing and Analysis, 6, 10, 1069-75, (2014)