The exposome in molecular epidemiology:
Towards a more global approach to evaluate exposures to disease risk factors

Augustin SCALBERT
Biomarkers Group
International Agency for Research on Cancer
Lyon, France
Causes of cancer are largely environmental

>600,000 cancers among parents
92,000 among offspring

Czene et al., 2002, *Int J Cancer*
Known and unknown environmental causes of cancers

- Established causes: infectious agents, smoking, alcohol, diet, lack of physical exercise
- 65% of cancer deaths unexplained

Danaei et al., 2005, Lancet
Exposome

Editorial

Complementing the Genome with an “Exposome”: The Outstanding Challenge of Environmental Exposure Measurement in Molecular Epidemiology

Christopher Paul Wild
Molecular Epidemiology Unit, Centre for Epidemiology and Biostatistics, Leeds Institute of Genetics, Health and Therapeutics, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom

Wild et al., 2005, CEBP

- The totality of environmental exposures received by an individual during life
- ‘A collection of environmental factors, such as stress and diet, to which an individual is exposed and which can have an effect on health’ (Collins)
Exposome-Wide Association Studies (EWAS)

Exposome = \sum \text{exposures}

(Nested) case-control studies

Disease risk

Association with disease risk

- Metabolome-wide, environmental-wide, nutrient-wide association studies (MWAS, EWAS, NWAS)
Dietary patterns and disease risk

Dietary patterns

Colorectal cancer incidence

Pradhan et al., 2013, *Plos ONE*

GLOBOCAN, 2012

International Agency for Research on Cancer
The components of dietary patterns

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat</td>
<td>Fruit and vegetables</td>
</tr>
<tr>
<td>SFA</td>
<td>Fruits (and nuts)</td>
</tr>
<tr>
<td>Ratio of MUFA or PUFA to SFA</td>
<td>Vegetables</td>
</tr>
<tr>
<td>PUFA</td>
<td>Legumes (and nuts and seeds)</td>
</tr>
<tr>
<td>Trans fatty acids</td>
<td>Nuts (and soya)</td>
</tr>
<tr>
<td>Protein</td>
<td>(Whole) cereals/grains (Coarse) bread</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>Meat (and meat products)</td>
</tr>
<tr>
<td>Complex carbohydrates</td>
<td>Ratio of white to red meat</td>
</tr>
<tr>
<td>(Cereal) fibre</td>
<td>Red and processed meat</td>
</tr>
<tr>
<td>Mono- and disaccharides</td>
<td>Poultry</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Fish</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Milk (and dairy products)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>High fat dairy</td>
</tr>
<tr>
<td>Sodium</td>
<td>Olive oil</td>
</tr>
<tr>
<td>Calcium</td>
<td>Cheese</td>
</tr>
<tr>
<td>Iron</td>
<td>Red wine</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Butter, margarine, animal fat</td>
</tr>
<tr>
<td>Ratio of carbohydrates to protein to fat</td>
<td>Sweets/sweet beverages</td>
</tr>
</tbody>
</table>

- Traditionally measured with dietary questionnaires
- Number of bias and errors in the measurements

Waijers et al., 2007, BJN
A first nutrient-wide association study

Nutrients and blood pressure associations in the INTERMAP cohort

- Alcohol
- Vegetable protein
- Total fiber
- Magnesium
- Phosphorus

Largely based on nutrient intake data

Tzoulaki et al., 2013, *Circulation*
Measurement of the exposome

External exposome

Internal exposome

Environmental and personal measurements

Biomarkers
The blood exposome

The internal exposome

All biologically active chemicals in the internal environment (endogenous and exogenous chemicals in human blood)

Rappaport & Smith, 2010, Science
• **Exposome**: The totality of environmental exposures received by an individual during life

• **Metabolome**: The complete collection of small molecular weight metabolites in a cell, tissue, biofluid or organism
First EWAS in a prospective cohort on pancreatic cancer

Four prospective cohorts (HPFS, NHS, PHS, WHI)
453 cases, 898 controls
Plasma samples
Avg. follow-up time: 8.7 yrs
83 polar metabolites measured by LC-ESI-MS-MS
(central metabolism and amino acid metabolism)

- Isoleucine, leucine and valine significantly increased after correction for multiple-hypothesis testing
- Association independent of intermediate development of diabetes

Expsome-Wide Association Studies
NHANES data

NHANES cohorts
266 environmental factors
in urine or plasma
Fasting glucose

US$ 40,000 per sample
The food metabolome

Exposures

Diet and dietary supplements

Food sp. 1
Food sp. 2
Food sp. 3
Food sp. 4

Exposures

Food metabolome

Diet

Dietary supplements

Food additives

Contaminants

Microbial metabolism

Host metabolism

Endogenous metabolome

Drug metabolome

Pollutant metabolome

FooDB, the most comprehensive database on food constituents

• 27,509 compounds known in foods
Biomarkers of citrus fruit intake

4 volunteers
Orange or grapefruit juice (600 ml)
Urine
UPLC-QToF

• 12 discriminating metabolites
  • Proline betaine, hydroxyproline betaine
  • Naringenin 7-O glucuronide, hesperetin 3’-O-glucuronide
  • Limonene 8,9-diol glucuronide, nootkatone 13,14-diol glucuronide

Pujos-Guillot et al., 2013, J. Proteome Res.
# Metabolomics and the food metabolome in acute intervention studies

<table>
<thead>
<tr>
<th>Food</th>
<th>Biospecimens</th>
<th>Analytical method</th>
<th>Biomarkers</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrus fruits</td>
<td>Urine</td>
<td>NMR</td>
<td>Proline betaine</td>
<td>Heinzmann, 2010</td>
</tr>
<tr>
<td></td>
<td>Urine</td>
<td>MS</td>
<td>Proline betaine, 4-hydroxyproline betaine</td>
<td>Lloyd, 2011</td>
</tr>
<tr>
<td></td>
<td>Urine</td>
<td>MS</td>
<td>Proline betaine, 4-hydroxyproline betaine, limonene 8,9-diol GlcUA, nootkatone 13,14-diol GlcUA, hesperetin GlcUA, naringenin GlcUA, N-methyltyramine sulfate</td>
<td>Pujos-Guillot, 2013</td>
</tr>
<tr>
<td>Raspberry</td>
<td>Urine</td>
<td>MS</td>
<td>Caffeoyl sulfate, methylepicatechin sulfate</td>
<td>Lloyd, 2011</td>
</tr>
<tr>
<td>Cruciferous vegetables</td>
<td>Urine</td>
<td>NMR</td>
<td>S-Methyl-L-cystein sulfoxide</td>
<td>Edmans, 2011</td>
</tr>
<tr>
<td>Wholegrain rye</td>
<td>Urine</td>
<td>MS</td>
<td>3-(3,5-Dihydroxyphenyl)-1-propanoic acid sulfate, enterolactone GlcUA, 2-aminophenol sulfate</td>
<td>Bondia-Pons, 2013</td>
</tr>
<tr>
<td>High-fiber diet</td>
<td>Plasma</td>
<td>MS</td>
<td>2-Aminophenol sulfate, 2,6- dihydroxybenzoic acid</td>
<td>Johansson-Persson, 2013</td>
</tr>
<tr>
<td>Oily fish</td>
<td>Urine</td>
<td>MS</td>
<td>Anserine, methylhistidine, TMAO</td>
<td>Lloyd, 2011</td>
</tr>
<tr>
<td>Cocoa</td>
<td>Urine</td>
<td>MS</td>
<td>Vanilloyl glycine, trigonelline, 3,5-diethyl-2-methylpyrazine, epicatechin sulfate, theobromine</td>
<td>Llorach, 2009, 2010</td>
</tr>
<tr>
<td>Coffee</td>
<td>Urine</td>
<td>MS</td>
<td>Caffeoylquinic acid sulfate, caffeoylquinic acid lactone sulfate, caffeic acid sulfate, feruloyl glyicine</td>
<td>Stalmach, 2009</td>
</tr>
<tr>
<td></td>
<td>Plasma</td>
<td>MS</td>
<td>Feruloylquinic acid lactone sulfate,</td>
<td>Redeuil, 2011</td>
</tr>
<tr>
<td>Tea</td>
<td>Urine</td>
<td>NMR</td>
<td>Hippuric acid, gallic acid, 1,3-dihydroxyphenyl-2-O-sulfate</td>
<td>Daykin, 2005</td>
</tr>
<tr>
<td>Nuts</td>
<td>Urine</td>
<td>MS</td>
<td>10-Hydroxy-decenoic acid, 4,6-diynoic acid sulfate, tridecadienoic/tridecynoic acid, GlcUA, dodecanedioic acid</td>
<td>Tulipani, 2011</td>
</tr>
<tr>
<td>Wine</td>
<td>Urine</td>
<td>NMR</td>
<td>Tartrate, EtOH, mannitol</td>
<td>Vázquez-Fresno, 2012</td>
</tr>
</tbody>
</table>

---

International Agency for Research on Cancer

World Health Organization

Scalbert et al., 2014, AJCN
The food metabolome in a cross-sectional study in EPIC

EPIC

- 520,000 participants
- 23 centres in 10 Western European countries
- Areas with varying cancer rates
- Heterogeneity of lifestyle habits
- Food Frequency Questionnaires (FFQ) detailed, validated, country-specific
- Plasma samples

EPIC calibration study

- 36,900 participants
- 24-hr dietary recalls (EPIC-Soft)
- 24-hr urine samples (n=1,103)
Metabolic profiles and food intake

481 subjects from 4 countries
24-hr Dietary recalls
24-hr Urine samples
High-resolution mass spectrometry (UPLC QTof, neg ionization)
Iterative regression analyses

- 14,000 mass spectrometry feature detected
- 2,272 features correlated to intake of six different foods

Edmands et al., 2014, *Bioinformatics*
Edmands et al., 2014, *Anal Chem*
Edmands et al., submitted
Dietary polyphenols

- > 500 polyphenols in >450 foods
- Often specific of a particular food or food group
- 60,000 content values in foods

http://www.phenol-explorer.eu

Neveu et al., 2010, Database
Perez-Jimenez et al., 2010, JAFC
Rothwell et al., 2014, Database
Phenol-Explorer - Polyphenol metabolites

- 375 polyphenol metabolites
- Human subjects and experimental animals
- Filiation between parent polyphenols and metabolites documented

Rothwell et al., 2012, *Database*

Rothwell et al., in preparation
Polyphenol metabolites as dietary biomarkers in EPIC

- 83 metabolites associated to the consumption of six polyphenol-rich foods

Edmands et al., submitted
Selection of best exposure biomarkers

- 6 polyphenol metabolites selected as best predictors of food intake

Edmands et al., submitted
Different metabolomic approaches

<table>
<thead>
<tr>
<th></th>
<th>Targeted metabolomics</th>
<th>Untargeted metabolomics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative analyses*</td>
<td>50-200 metabolites</td>
<td>--</td>
</tr>
<tr>
<td>Semi-quantitative analyses</td>
<td></td>
<td>Up to 15,000 MS features</td>
</tr>
</tbody>
</table>

* Requires calibration with appropriate chemical standards
Welcome to Exposome-Explorer

Exposome-Explorer is a database on biomarkers of environmental exposure.

We first started the development of the database with dietary biomarkers. We systematically collected information in the scientific literature on all biomarkers that have been measured in population studies. We included in the database detailed information on each study and in particular about correlations between biomarkers and dietary intake.

You can try the Biomarkers page and click on a particular literature source to see the full volume of data collected.

We plan to add more data as follows:

- Reliability studies on repeated samples
- Dose-response relationships (from selected intervention studies)
- Information on metabolic pathways leading to the biomarkers

We also plan to extend the database to other exposure biomarkers (like air-pollution and water-pollution biomarkers).

Statistics (Oct. 2014)

- 403 peer-reviewed publications analyzed
- 438 biomarkers
- 10,474 concentration values
- 8,090 correlation values with dietary exposures
Exposome-Explorer
438 biomarkers of exposures (Oct 2014)

306 environmental pollutants

PBDEs

PCDDs

PCBs

319 concentration values

PAHs

PCDFs

131 dietary compounds

POLYPHENOLS

FATTY ACIDS

CAROTENOIDs
## A panel of dietary biomarkers for targeted nutrient-wide association studies

<table>
<thead>
<tr>
<th>Chemical class</th>
<th>Biomarkers (#)</th>
<th>Food/nutritent intake</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino acids</td>
<td>2</td>
<td>Proteins, meat, fish</td>
<td>1-Methylhistidines</td>
</tr>
<tr>
<td>Organic acids</td>
<td>1</td>
<td>Proteins</td>
<td>Taurine</td>
</tr>
<tr>
<td>Aliphatic acyclic compounds</td>
<td>1</td>
<td>Proteins</td>
<td>Urea</td>
</tr>
<tr>
<td>Fatty acids</td>
<td>35</td>
<td>Fish, milk, milk products, beef meat</td>
<td>DHA</td>
</tr>
<tr>
<td>Vitamins</td>
<td>11</td>
<td>Fruits, vegetables, citrus fruits</td>
<td>Vitamin C</td>
</tr>
<tr>
<td>Inorganic compounds</td>
<td>6</td>
<td>Milk</td>
<td>Iodine</td>
</tr>
<tr>
<td>Carotenoids</td>
<td>6</td>
<td>Fruits, vegetables, carrot, tomato, citrus fruits</td>
<td>Lycopene</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>4</td>
<td>Apple, tea, fruits, fruit &amp; vegetables</td>
<td>Quercetin</td>
</tr>
<tr>
<td>Flavanones</td>
<td>3</td>
<td>Orange, grapefruit, citrus fruits</td>
<td>Hesperetin</td>
</tr>
<tr>
<td>Dihydrochalcones</td>
<td>1</td>
<td>Apple</td>
<td>Phloretin</td>
</tr>
<tr>
<td>Isoflavones</td>
<td>7</td>
<td>Soy milk, soy solid foods, soy proteins</td>
<td>Daidzein</td>
</tr>
<tr>
<td>Phenolic acids</td>
<td>5</td>
<td>Tea, coffee, wine, orange, apple</td>
<td>Gallic acid</td>
</tr>
<tr>
<td>Lignans</td>
<td>2</td>
<td>Vegetables, dietary fibre</td>
<td>Enterolactone</td>
</tr>
<tr>
<td>Stilbenes</td>
<td>1</td>
<td>Wine</td>
<td>Resveratrol</td>
</tr>
<tr>
<td>Alkylresorcinols</td>
<td>6</td>
<td>Wholegrain cereals, dietary fibre</td>
<td>5-Heptadecylresorcinol</td>
</tr>
<tr>
<td>Food contaminants</td>
<td>3</td>
<td>Fish</td>
<td>Mercury</td>
</tr>
<tr>
<td>Cooking products</td>
<td>2</td>
<td>Grilled meat</td>
<td>1-hydroxypyrene glucuronide</td>
</tr>
<tr>
<td>Enzymes</td>
<td>3</td>
<td>Alcoholic beverages</td>
<td>ALAT</td>
</tr>
</tbody>
</table>
Environmental pollutants present at (very) low concentrations in blood

Sensitivity of analytical instruments

Metabolomics and pesticide exposures

Table 3 Variation of signals as a result of exposure

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>p-value</th>
<th>(Urban + low)/medium</th>
<th>(Urban + low)/high</th>
<th>Medium/high</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl-2-(2-hydroxyphenyl)-3-methoxyacrylate sulfate</td>
<td>$6.5 \times 10^{-6}$</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>2-Methyl-2-phenylpropanoic acid</td>
<td>$2.2 \times 10^{-5}$</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>Methyl-2-(2-hydroxyphenyl)-3-methoxyacrylate glucuronide (1)\textsuperscript{a}</td>
<td>$9.6 \times 10^{-5}$</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>Methyl-2-(2-hydroxyphenyl)-3-methoxyacrylate glucuronide (2)\textsuperscript{a}</td>
<td>$6.3 \times 10^{-5}$</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>3,3-Dimethyl-2,3-dihydro-1-benzofuran-7-ol sulfate</td>
<td>0.0197</td>
<td>n.s.</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>3,3-Dimethyl-2,3-dihydro-1-benzofuran-7-ol glucuronide</td>
<td>0.0409</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>7-Hydroxy-2,2-dimethyl-1-benzofuran-3(2H)-one glucuronide</td>
<td>0.0033</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
<tr>
<td>2-(4-Hydroxyphenoxy)propanoic acid sulfate (2)\textsuperscript{a}</td>
<td>0.0404</td>
<td>+</td>
<td>+</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

- 7 pesticide metabolites identified in urine and associated to proximity of cereal crop land

Environmental contaminants and untargeted metabolomics

<table>
<thead>
<tr>
<th>Environmental chemical</th>
<th>Detected $m/z$</th>
<th>Delta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-tyrosine (herbicide)$^a$</td>
<td>182.0805</td>
<td>0.0007</td>
</tr>
<tr>
<td>Carbendazim; mercarzole (carcinogen)$^a$</td>
<td>192.0741</td>
<td>0.0026</td>
</tr>
<tr>
<td>N-butyl-benzenesulfonamide (plasticizer)$^{ab}$</td>
<td>214.0892</td>
<td>0.0004</td>
</tr>
<tr>
<td>Diethyl phthalate (plasticizer)$^{ab}$</td>
<td>223.0937</td>
<td>0.0028</td>
</tr>
<tr>
<td>Pirimicarb (insecticide)$^a$</td>
<td>239.1482</td>
<td>0.0021</td>
</tr>
<tr>
<td>Diisopropyl phthalate (plasticizer)$^{ab}$</td>
<td>251.1270</td>
<td>0.0008</td>
</tr>
<tr>
<td>Dibutyl phthalate (plasticizer)$^{ab}$</td>
<td>279.1574</td>
<td>0.0017</td>
</tr>
<tr>
<td>Butylnbenzyl phthalate (plasticizer)$^{ab}$</td>
<td>313.1417</td>
<td>0.0018</td>
</tr>
<tr>
<td>Triphenyl phosphate (flame retardant)$^{ab}$</td>
<td>327.0766</td>
<td>0.0015</td>
</tr>
<tr>
<td>Di-n-hexyl phthalate (plasticizer)$^{ab}$</td>
<td>335.2176</td>
<td>0.0014</td>
</tr>
<tr>
<td>Chlorsulfuron (herbicide)$^a$</td>
<td>358.0372</td>
<td>0.0008</td>
</tr>
<tr>
<td>Imazalil nitrate$^{ab}$</td>
<td>359.0407</td>
<td></td>
</tr>
<tr>
<td>Di-n-heptyl phthalate (plasticizer)$^{ab}$</td>
<td>363.2503</td>
<td>0.0026</td>
</tr>
<tr>
<td>Di(2-ethylhexyl) adipate (plasticizer)$^{ab}$</td>
<td>371.3134</td>
<td>0.0022</td>
</tr>
<tr>
<td>Surfentrazone (herbicide)$^{ab}$</td>
<td>386.9885</td>
<td>0.0007</td>
</tr>
<tr>
<td>Diisooctyl phthalate (plasticizer)$^{ab}$</td>
<td>391.2818</td>
<td>0.0025</td>
</tr>
<tr>
<td>Macluraxanthone (insecticide)$^{ab}$</td>
<td>395.1526</td>
<td>−0.0037</td>
</tr>
<tr>
<td>Endosulfan (insecticide)$^a$</td>
<td>404.8213</td>
<td>0.0028</td>
</tr>
<tr>
<td>Diisononyl phthalate (plasticizer)$^{ab}$</td>
<td>419.3134</td>
<td></td>
</tr>
<tr>
<td>Diisodecyl phthalate (plasticizer)$^{ab}$</td>
<td>447.0195</td>
<td></td>
</tr>
</tbody>
</table>

Human plasma samples
LC-FTICR-MS

Soltow et al., 2011, Metabolomics
# Measuring the exposome

## Analytical challenges

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>High complexity of the exposome</td>
<td>Improved annotation of the exposome (human metabolites)</td>
</tr>
<tr>
<td>Low concentrations of metabolites</td>
<td>Higher sensitivity</td>
</tr>
<tr>
<td>Low sample volumes</td>
<td>Miniaturization of sample processing</td>
</tr>
<tr>
<td>Intra-individual variations along time</td>
<td>Repeated samples, Biomarkers with longer half-life</td>
</tr>
<tr>
<td>Large cohorts</td>
<td>Lower analytical run time</td>
</tr>
<tr>
<td></td>
<td>High robustness of the analytical workflow</td>
</tr>
<tr>
<td></td>
<td>Quantitative measurements</td>
</tr>
</tbody>
</table>

*International Agency for Research on Cancer*
Quantifying the exposome with differential isotopic labelling

- Dansylation of phenols and amines
- First application to a cohort study (38 dietary polyphenols)

Achaintre et al., in preparation
Exposome-Wide Association Studies (EWAS)

Blood exposome

(Nested) case-control studies

Disease risk

Association with disease risk

• Success for a truly agnostic approach in discovering novel disease risk factors will depend on our capacity to reliably measure the exposome

Chemicals, nutrients
## Metabolomics on various biospecimens

<table>
<thead>
<tr>
<th>Biospecimen</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma (heparin, citrate, EDTA)</td>
<td>Darghouh et al., 2011, <em>Blood</em></td>
</tr>
<tr>
<td>Serum</td>
<td></td>
</tr>
<tr>
<td>Red blood cells</td>
<td></td>
</tr>
<tr>
<td>Dried blood spots</td>
<td>Takeda et al., 2009, <em>NMR Biomed.</em>; Sugimoto et al., 2010, <em>Metabolomics</em></td>
</tr>
<tr>
<td>Saliva</td>
<td></td>
</tr>
<tr>
<td>Hair</td>
<td>Sulek et al., 2014, <em>Theranostics</em></td>
</tr>
</tbody>
</table>
Biomarkers and biospecimens in Exposome-Explorer

PBDEs

PCDDs

PCBs

Pesticides

PCDFs

PAHs

Adipose tissue
Hair
Breath...

POLYPHENOLS

FATTY ACIDS

CAROTENOIDS
Measuring the exposome

Conclusions

• A minor fraction of the exposome so far measured
• To replace or complement classical methods of assessment of exposure to disease risk factors
  • Missing data in questionnaires
  • Improved measurements
• To identify new risk factors for cancer and other diseases
• Methodological progress still needed to apply metabolomics to cohort studies
Acknowledgments

Claudine Manach
Craig Knox
David Wishart
Liang Li
Rashmi Sinha
Erikka Loftfield
Neal Freedman
Paolo Vineis
Marc Gunter
Tim Key
Bernardo Bonnani

Chris Wild
Isabelle Romieu
Mazda Jenab
Pietro Ferrari
Nadia Slimani

Veronique Chajes
Nicole Suty
David Achaintre
Sabina Rinaldi
Vanessa Neveu
Beatrice Vozar
Steve Rappaport
Joe Rothwell
Augustin Scalbert
Dinesh Barupal
Alice Moussy

INRA
University of Alberta
NATIONAL CANCER INSTITUTE
Imperial College London
UNIVERSITY OF OXFORD
dkfz.
World Health Organization
Epic
NutriTech
Exposomics
EurocanPlatform