E02- Metabolism of Xenobiotics

Head : Daniel ZALKO

- Metabolic **Bioactivation / Détoxification** of food-chain contaminants
- Understanding the **mechanisms of Xenobiotics biotransformation, in relation with their toxicity** and with the risks faced by consumers
- Endocrine disrupters (plasticizers, pesticides, flame retardants) and genotoxicants
- Modelisation of **metabolic networks** involved in the disruption of *in vitro* (cellular models) and *in vivo* (organism) biological systems
- Consequences of **low dose exposure** to **endocrine disrupters** on the homeostasis of biological systems

Main projects and results :

Bisphenols

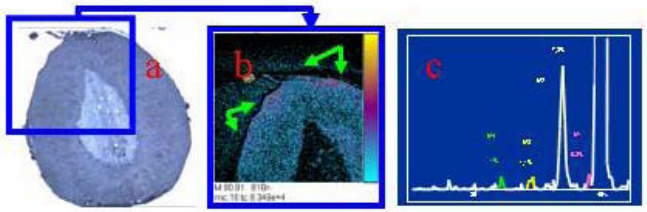
- Demonstration of the trans-placental passage of bisphenol A and its metabolites
- Long term disruption of metabolism following *in utero* exposure to very low doses of BPA (serum, brain, liver) : metabolomics
- Biological activity of metabolites: halogenated bisphenols are PPARγ ligands

Pesticides and polycyclic aromatic hydrocarbons

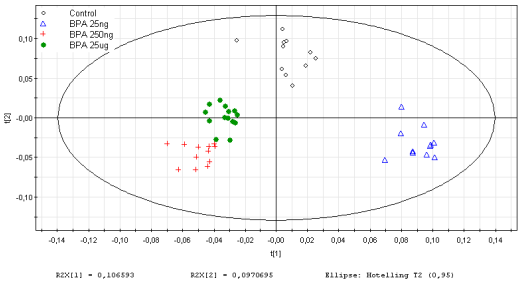
- Development of the H2AX genotocicity test
- Links between metabolism and genotoxicity : single contaminant and mixture exposures

Brominated flame retardants

- Demonstration of mother and newborn exposure (perinatal exposure in France)
- Two endocrine glands (adrenals and ovaries) are the main targets of PBDE



Adrenal glands of rats dosed DBDE (a); image of tissue residues of DBDE using ToF-SIMS (b); Metabolic profile of an extract of adrenals in a rat orally dosed with ^{14}C-DBDE. [INRA-Mex/CNRS/ENVT]



Metabonomic analysis of brain extracts from CD1 mice aged 21 days, after mother's exposure to **Bisphenol A**. A remarkable separation is obtained For the different doses of Bisphenol A to which the mothers were exposed. [INRA-MeX/TUFTS]

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Perspectives : to decipher the **mechanisms of toxicity** by which **major food contaminants** exert their effects (metabolic bioactivation and genotoxicity). To evaluate their impact on the expression of metabolic capabilities in biological systems, and the perturbation of these systems by chemical contaminants of the food chain (« omics » approaches and metabolic networks).

Collaborations : INSERM U896 (Montpellier) & U625 (Rennes); ICSN/CNRS; Institut de Génomique Fonctionnelle de Lyon, ENS (Lyon); LABERCA (Nantes); MNHN (Paris); University of Missouri-Columbia (USA); Tufts University, Boston (USA), Université de Sherbrooke (Québec).

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