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Metabonomic evaluation of oxaliplatin hepatotoxicity by comparison with a sinusoidal obstruction syndrome (SOS) model

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Colorectal cancer (CRC) is the second cancer diagnosed in humans. The main curative treatment remains the surgery. However, when metastases are suspected, surgery is followed by a preventive chemotherapy using Oxaliplatin (OXA). Under Oxaliplatin, some patients develop a treatment-related hepatotoxicity known as Sinusoidal Obstruction Syndrome (SOS). Such hepatic damage is barely detected during or after chemotherapy due to a lack of effective diagnostic procedures, but liver biopsy. In our laboratory, a predictive rat model of SOS was built using a metabonomic approach that is based on the ^{1}H-NMR spectroscopy analysis of urine samples collected from rats exposed to monocrotaline (MCT), a SOS model toxin. In the present study, OXA was evaluated in this predictive model.Wistar rats (4/group) received saline or sub-toxic doses of the tested drug (OXA or MCT) once a day during four consecutive days. Urine samples were collected daily during seven days and analyzed by ^{1}H NMR spectroscopy. Principal component analysis (PCA) was applied to the reduced data set. Rats treated with OXA or MCT showed significant urine changes as compared to controls, mainly decreases in citrate, alpha-ketoglutarate, succinate and hippurate and increases in taurine, creatine, creatinine, amino acids and ketone bodies. Those metabolic changes are consistent with liver injury. In addition, PCA revealed an overlap between the metabolic signatures in OXA- and MCT-treated rats, suggesting similar cellular mechanisms of toxicity. After validation, urine biomarkers identified in the MCT animal model of SOS could be used to detect and follow OXA-induced hepatotoxicity in patients under chemotherapy.

Biography

Raphaël Conotte is a Master in Biology and is currently working as a phD student in the laboratory of Human Biology and Toxicology of Mons University (Belgium). His research domain concerns the chemotherapy effects in the renal cancer and the identification of efficiency and toxicity biomarkers by metabonomic approach.

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