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# *Modelling intrahepatic metabolic rewiring during the onset of obesity using arterio-venous blood metabolomics profiles*

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## **Introduction**

General introduction to biological or methodological context (500 characters maximum spaces included)

The metabolite composition of the blood inflowing and outflowing a tissue reflects its metabolic function, with consumed (resp. released) metabolites being in higher (resp. lower) concentration in arterial inflow than venous outflow. The objective of this study was to perform a global metabolic profiling of plasma from incoming and outgoing hepatic vessels using NMR on high fat/high sugar (HFHS)-fed minipigs to explore how the hepatic metabolism is modulated during the onset of obesity [1].

## **Technological and methodological innovation**

500 characters maximum spaces included

The originality of our approach was to translate NMR arterio-venous metabolic profiles into utilization and release fluxes that we integrated in a tuned hepatic genome-scale metabolic network model to simulate fluxes through intra-tissular metabolic reactions. By setting constraints on model exchange reactions to enforce uptake and release of metabolites fitting the experimental data and using *in silico* flux calculation methods we could predict associated changes in intrahepatic metabolic fluxes.

## **Results and impact**

500 characters maximum spaces included

The interest and novelty of the presented approach is to take advantage of accessible circulating metabolites across a tissue to computationally predict rewiring in its metabolism and changes in consumed and released metabolites that could constitute biomarkers of intra-tissular metabolic modulations. Using this metabolic network modelling strategy, we predict that HFHS is associated with changes in tryptophan catabolism [2], which were further supported by biochemical and molecular analyses.

## **References**

Max 5

[1] Polakof S *et al.* 2018. Eur J Nutr. 57(1):119-35

[2] Poupin N *et al.* 2019. Sci Reports. 9(1):12557

## **Keywords**

metabolic networks modelling; flux analysis; NMR; arterio-venous differences; obesity; mini-pigs