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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