



**HAL**  
open science

## Modelling the muscle metabolic response in anabolic and catabolic states using arterio-venous blood metabolomics profiles

Nathalie Poupin, Florence A Castelli, Emeline Chu-Van, Didier Remond, Dominique Dardevet, Isabelle Savary-Auzeloux, François Fenaille, Fabien Jourdan, Sergio Polakof

### ► To cite this version:

Nathalie Poupin, Florence A Castelli, Emeline Chu-Van, Didier Remond, Dominique Dardevet, et al.. Modelling the muscle metabolic response in anabolic and catabolic states using arterio-venous blood metabolomics profiles. 8. Conference on Constraint-Based reconstruction and Analysis (COBRA 2022), Sep 2022, Galway, Ireland. hal-03807737

**HAL Id: hal-03807737**

**<https://hal.inrae.fr/hal-03807737>**

Submitted on 10 Oct 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## *Modelling the muscle metabolic response in anabolic and catabolic states using arterio-venous blood metabolomics profiles*

Nathalie Poupin<sup>1</sup>, Florence Castelli<sup>2</sup>, Emeline Chu-Van<sup>2</sup>, Didier Rémond<sup>3</sup>, Dominique Dardevet<sup>3</sup>, Isabelle Savary-Auzeloux<sup>3</sup>, François Fenaille<sup>2</sup>, Fabien Jourdan<sup>1</sup>, Sergio Polakof<sup>3</sup>

<sup>1</sup>UMR1331 Toxalim, Université de Toulouse, INRAE, ENVT, INP-Purpan, UPS, Toulouse, France.

<sup>2</sup>Université Paris Saclay, CEA, INRAE, Médicaments et Technologies pour la Santé (MTS), MetaboHUB, 91191 Gif-sur-Yvette, France.

<sup>3</sup>Université Clermont-Auvergne, INRAE, UMR1019, Unité Nutrition Humaine, Clermont-Ferrand, France.

The *in vivo* and kinetic investigation of tissue metabolism remains currently challenging, due essentially to ethical and technical issues preventing from obtaining repeated tissue biopsies on the same individual. In this study, we propose to combine plasma metabolomics measurements with metabolic-network based modelling, to investigate the muscle metabolism in anabolic and catabolic situations. Our underlying hypothesis is that the metabolite composition of the blood inflowing and outflowing the muscle reflects its metabolic function, with consumed (respectively released) metabolites being in higher (respectively lower) concentration in arterial inflow than venous outflow.

We therefore performed a global metabolomic profiling of plasma from incoming and outgoing muscle vessels, in hindlimb multicatheterized minipigs, using liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS). Thanks to this multi-catheterized experimental setting, blood sampling was performed in conscious animals at the fasting state and at different times during the postprandial period, in a normal vs. catabolic situation (induced by a glucocorticoid treatment).

Arterio-venous metabolic profiles obtained from plasma samples were translated into utilization and release fluxes, which we then integrated into a genome-scale metabolic network to simulate fluxes through intra-muscle metabolic reactions. The calculated metabolite ratios between arterial and venous blood allowed us to identify significantly released and consumed metabolites, which mainly belonged to amino acid and TCA cycle pathways. We used these experimental data to set constraints on exchange reactions of the metabolic network, enforcing uptake and release of the corresponding metabolites. We then applied *in silico* flux balance analysis methods to predict associated changes in intramuscular metabolic fluxes.

This allowed us to predict and explore the metabolic switch in the muscle from a catabolic (fasting) to an anabolic (postprandial) state, and to investigate how these changes were modulated in a pharmacologically induced catabolic situation, commonly observed in some pathophysiological states such as insulin-resistance, obesity, or ageing.