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<u>Title</u>: A scoping review: metabolomics signatures associated with animal or plant protein intake and their potential relation to cardiometabolic risk

Abstract

Objective: The dietary shift from animal protein (AP) sources to plant protein (PP) sources is promoted for both environmental and health reasons. Indeed, PP are associated to lower cardiovascular and diabetes risks compared to AP, but the underlying mechanisms remain mostly unknown. Metabolomics, which has a unique ability to provide an integrative snapshot of the metabolic status of an individual, is a valuable tool to investigate the different metabolic pathways activated by AP or PP intake and to provide biomarkers of their metabolic effects. This scoping review aimed at gathering and analyzing the available data on the metabolomics signatures associated to PP or AP intake, for discussing the metabolic effects underlying these signatures and their potential implication for cardiometabolic health.

<u>Methods</u>: We selected a total of 23 human studies comparing the urine, plasma or serum metabolomes associated to diets with contrasted AP and PP intakes, such as vegetarian and omnivore diets, and collected all discriminant metabolites across diets.

<u>Results:</u> Out of the 447 discriminant metabolites, 44 were repeatedly reported across studies, amino acids (AA) and AA-related products accounting for a high proportion. Branch-chained amino acids (BCAA), aromatic amino acids (AAA), glutamate, short-chained acylcarnitines and Trimethylamine-N-Oxide (TMAO) were associated to AP while glycine was associated to PP intake. TCA cycle intermediates and products from AAA gut microbiota degradation were also often reported, but the direction of their associations with AP or PP remained unclear. As regard to their implication for cardiometabolic health, BCAA, AAA, glutamate, short-chained acylcarnitines and TMAO are known to be associated to increased risk while glycine is rather associated with a decreased risk.

Conclusion: AP or PP intakes result in different metabolomics signatures, several metabolites being plausible candidates to at least partially explain their differential associations with cardiometabolic risk. Additional studies with a specific focus on protein type, deep dietary data and tight intake control are needed to better characterize the associated metabolic phenotype and understand how it could mediate AP or PP effects on cardiometabolic risk.

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