



HAL
open science

Toxic microbiome and chronic kidney disease: insights from the CKD-REIN cohort study

Manolo Laiola, Sandra Wagner, Laetitia Koppe, Islam Amine Larabi, Florence Thirion, Denis Fouque, Sophie Liabeuf, Emmanuelle Le Chatellier, Jean Claude Alvarez, Ziad A. Massy, et al.

► **To cite this version:**

Manolo Laiola, Sandra Wagner, Laetitia Koppe, Islam Amine Larabi, Florence Thirion, et al.. Toxic microbiome and chronic kidney disease: insights from the CKD-REIN cohort study. the 9th International Human Microbiome Consortium (IHMC) Congress, Nov 2022, Kobe, Japan. hal-04713459

HAL Id: hal-04713459

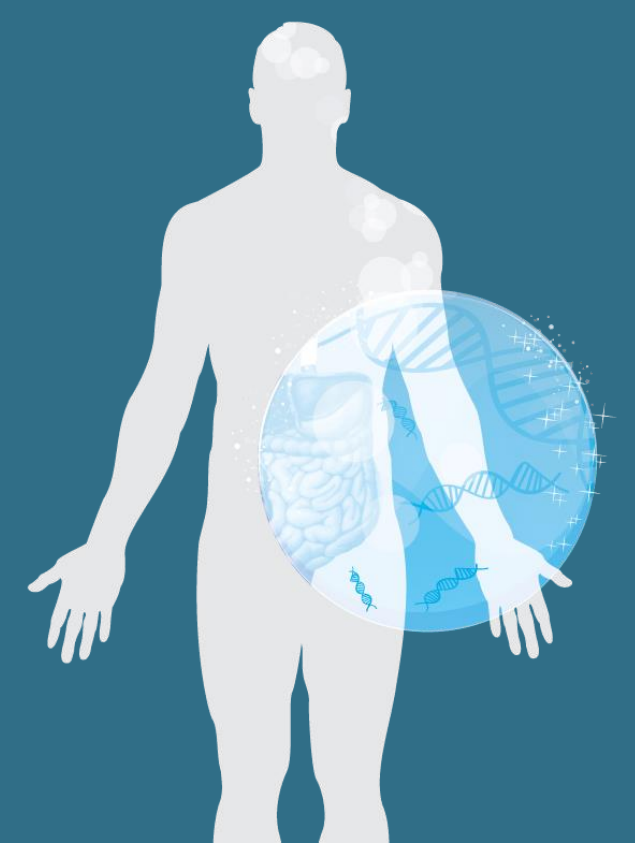
<https://hal.science/hal-04713459v1>

Submitted on 29 Sep 2024

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.

Public Domain



Manolo Laiola^a, Sandra Wagner^b, Laetitia Koppe^{c,d}, Islam Amine Larabi^e, Florence Thirion^a, Denis Fouque^{c,d}, Sophie Liabeuf^f, Emmanuelle Le Chatelier^a, Jean-Claude Alvarez^e, Ziad Massy^{g,h}, Bénédicte Stengel^h, Stanislav Dusko Ehrlich^{a,i}

Background

Chronic kidney disease (CKD) is often associated with alterations in gut microbiome composition and functions, particularly with food-derived proteins fermentation in the colon, leading to the production of uremic toxins [1,2]. Nevertheless, the identification of the relations between the aberrant and “toxic” microbiome, the CKD severity and the potential impact of diet have not been exhaustively explored in humans.

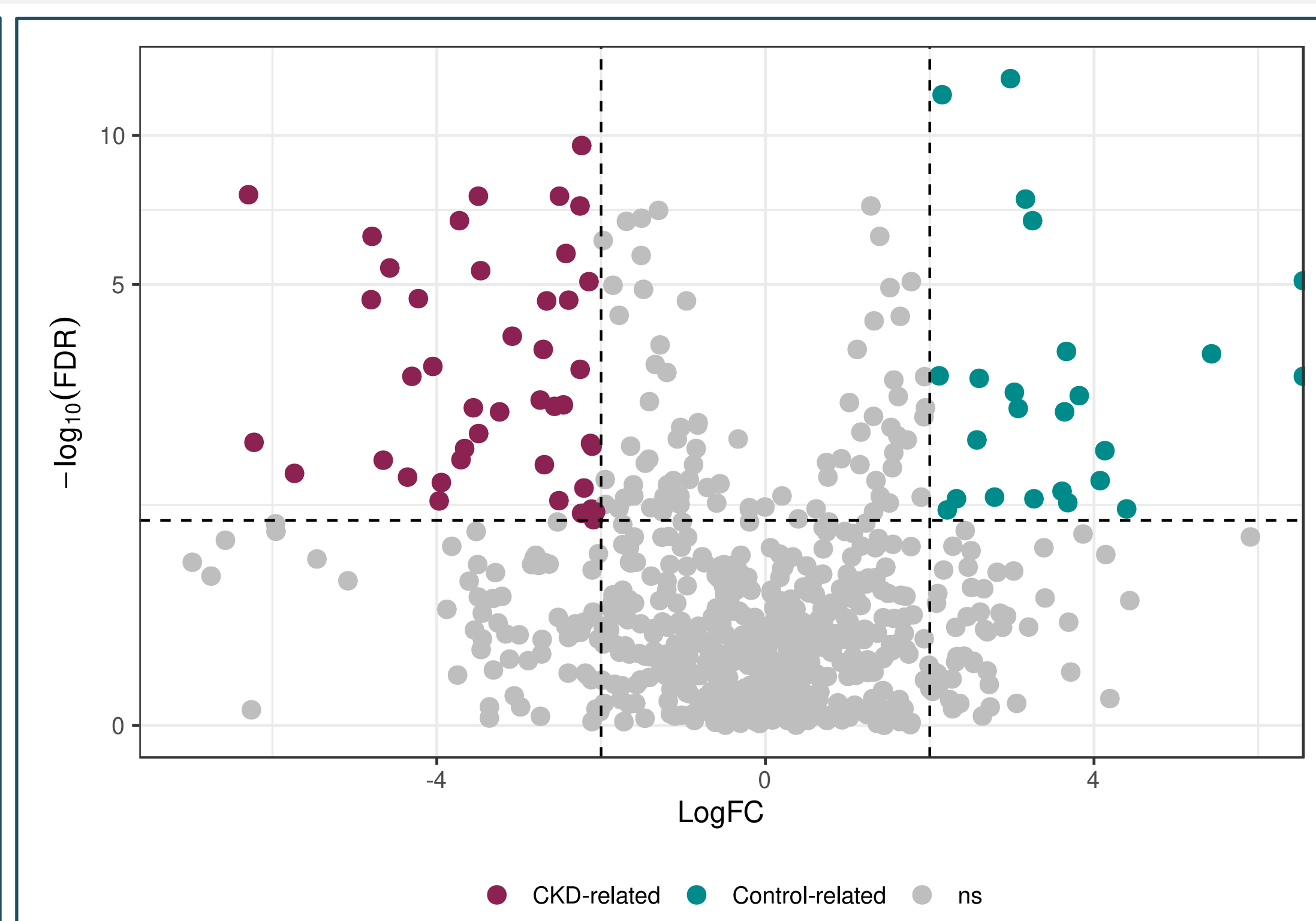
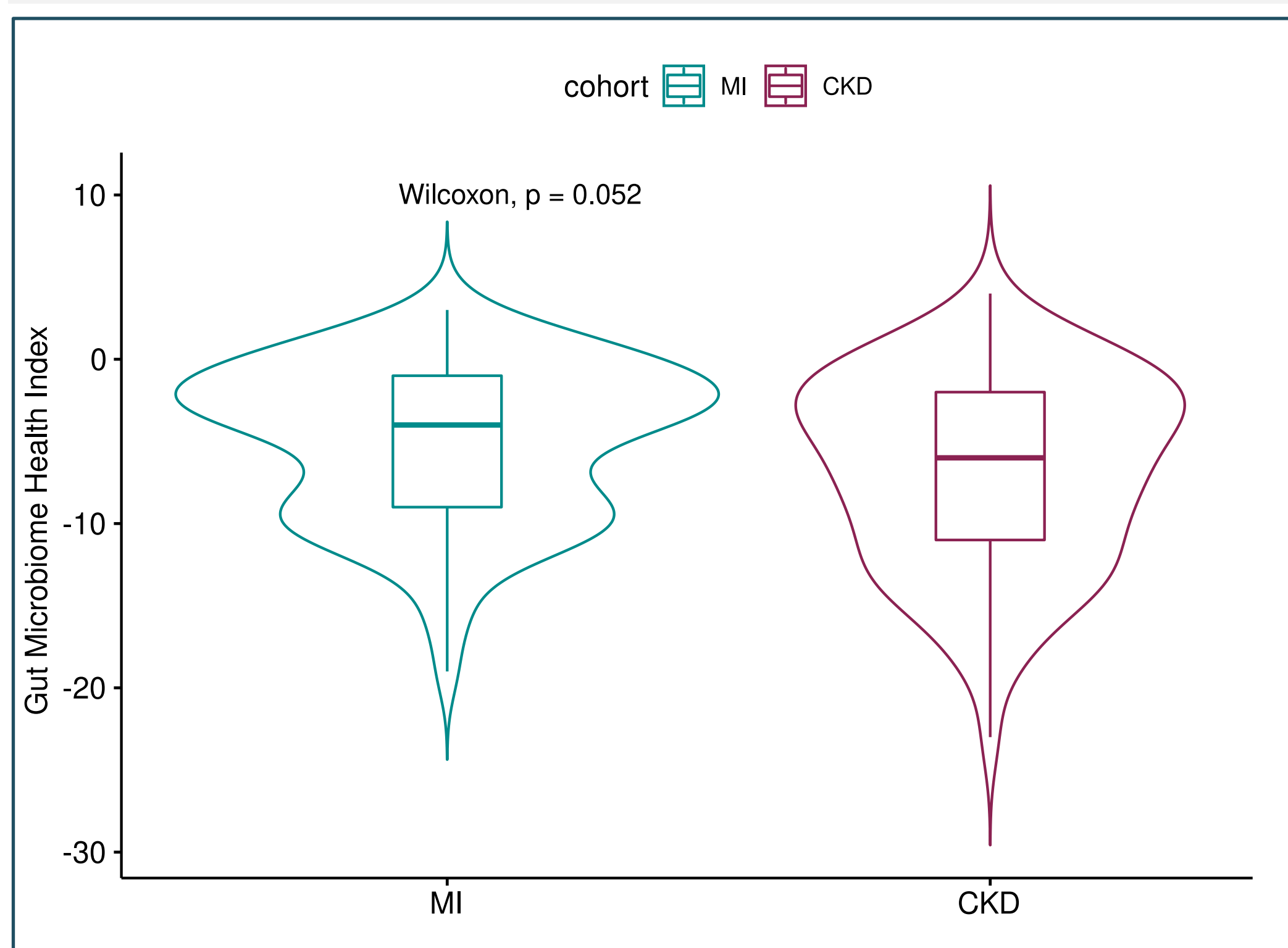
Aim

We investigated the associations between gut microbiome composition, blood uremic toxins, clinical metadata and food intake over a subsample of 240 patients (mean age, 68 [SD 11.6] years; 71% male) with non-dialysis CKD and an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² from the CKD-REIN study[3]. Moreover, an observational comparison with a healthy cohort (Milieu Interieur[4], n=938) was also performed to find out microbial biomarkers characterizing the gut microbiome-related toxicity in CKD.

Results

1 CKD vs Milieu Interieur

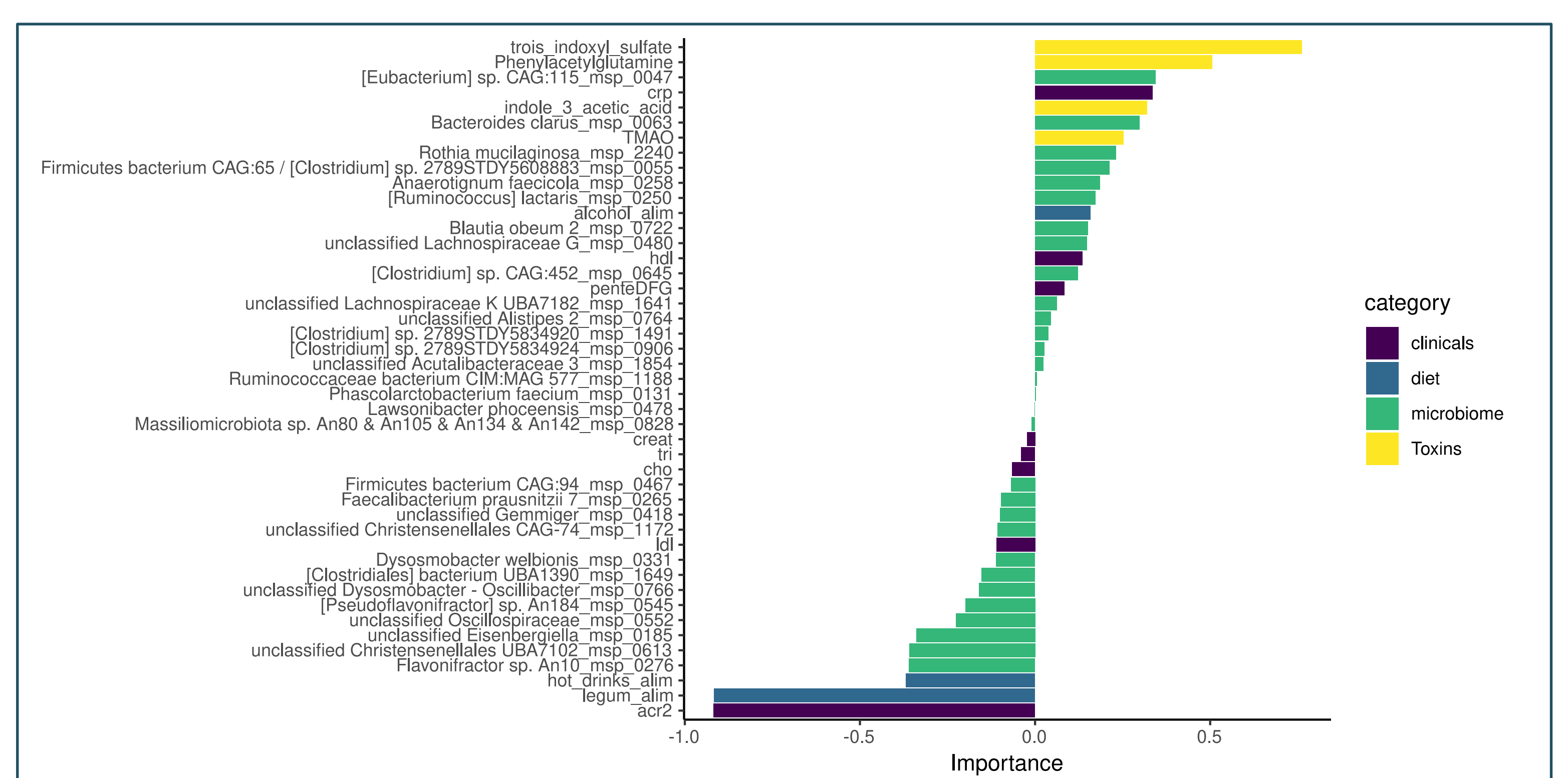
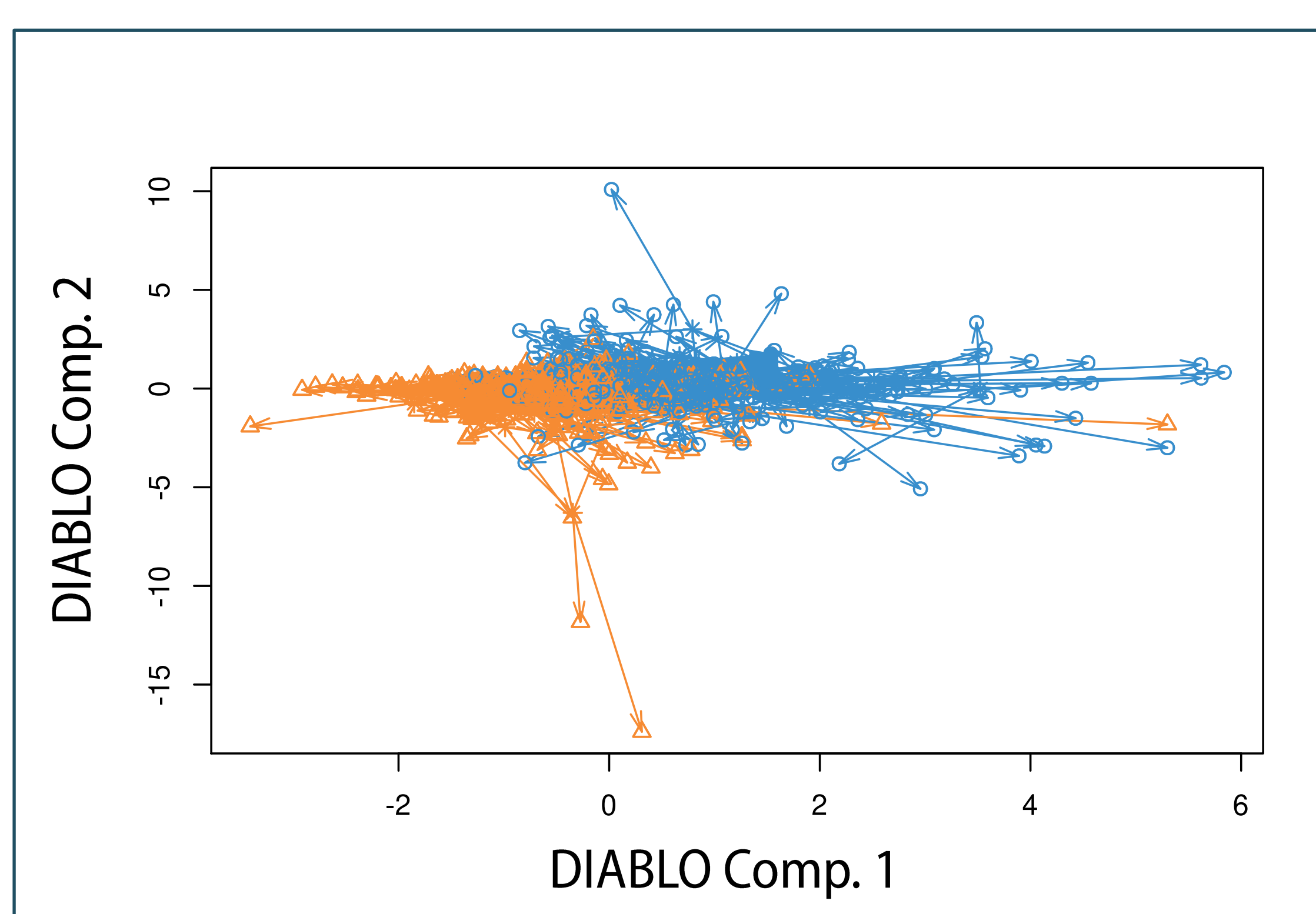
Using species level profiling, we observed that CKD patients showed a significant reduced gut microbiome health index compared to controls (left). Several CKD-related potential biomarkers were retrieved (center), like toxins producer species *Negativibacillus massiliensis* and *Victivallis vadensis* among others after adjusting for age, BMI, gender and diabetes condition as confounders (right). In addition, taxa belonging to *Enterocloster* and *Hungatella* clades (*Lachnospiraceae* family) were found negatively correlated to eGFR and positively associated with C-reactive protein (CRP) levels.



Species	Toxins producer	logFC	qvalue
msp_0432_unclassified Clostridiales 1h	Toxins producers	-6.291749	2.275183e-08
msp_0159_Victivallis vadensis	Toxins producers	-4.787769	5.056833e-07
msp_0092_Sutterella wadsworthensis	no	-3.944534	2.076163e-02
msp_0056_unclassified Enterocloster	Toxins producers	-3.705545	1.189990e-02
msp_0177_unclassified Enterocloster	no	-3.661100	8.313251e-03
msp_0009_Enterocloster boltaea	no	-3.555349	2.320354e-03
msp_0713_Enterocloster citroniae	Toxins producers	-2.741343	1.775263e-03
msp_1515_unclassified Enterocloster	no	-2.704590	2.467097e-04
msp_1143_unclassified Dysosmobacter - Oscillibacter	Toxins producers	-2.662817	2.439352e-05
msp_0780_unclassified Hungatella	no	-2.566754	2.206655e-03
msp_0930_unclassified Lachnospiraceae K UBA7182	no	-2.427789	1.564762e-06
msp_0151_Butyricimonas faecihominis	Toxins producers	-2.394813	2.349174e-05
msp_1641_unclassified Lachnospiraceae K UBA7182	Toxins producers	-2.257034	5.547415e-08
msp_1236_unclassified Hungatella	Toxins producers	-2.255165	5.629598e-04
msp_2277_Eubacterium sulci	no	-2.208554	2.380105e-02
msp_0820_unclassified Hungatella	no	-2.147764	8.523768e-06
msp_0360_Enterocloster asparagiformis = lavalensis	Toxins producers	-2.128461	7.164328e-03
msp_0037_Bacteroides salyersiae	Toxins producers	-2.116112	3.907476e-02
msp_0079_[Clostridium] sp. CAG-7	Toxins producers	-2.108854	7.774369e-03
msp_0203_Negativibacillus massiliensis	Toxins producers	-2.067592	4.158141e-02

2 Moderate vs Severe CKD phenotype

A supervised modelling for data integration was carried out to explore associations between multiomics' biomarkers differentiating moderate (n=130, eGFR ≥ 30 mL/min) and severe (n=110, eGFR < 30 mL/min) CKD phenotypes (left). In particular, severe-related taxa carrying genes involved in the production of metabolites causing uremic toxicity were linked to serum uremic toxins as indoxyl sulphate, trimethylamine-N-oxide, phenylacetylglutamine and kynurenic acid, along with CRP levels, alcohol consumption and low vegetables intake (right).



Conclusions

Our study highlights the important associations of gut microbiome composition and uremic toxins accumulations with CKD severity. Moreover, the findings might open to promising therapeutic strategy to diminish microbiome-related toxicity and to potentially attenuate CKD severity, by regulating the gut microbial configuration possibly through the modulating effect of dietary intakes.

