Title: Integrating Gut Microbiome and Metabolome Insights to Improve Outcomes in Kidney Disease and Transplantation

Nessrine Souai [1,2,], Oumaima Zidi [1,2], Amor Mosbah [1], Anis Bafoun [3], Imen Kosai[4], Jameleddine El Manaa[4] , Elias Asimakis [5], Panagiota Stathopoulou [5], Ameur Cherif [1] George Tsiamis [5] and Soumaya Kouidhi [1,*]

[1] Laboratory of Biotechnology and Valorisation of Bio-GeoRessources, Higher Institute of Biotechnology of Sidi Thabet, BiotechPole of Sidi Thabet, University of Manouba, Ariana 2020, Tunisia; nessrine.souai@fst.utm.tn (N.S.); oumaima.zidi@hotmail.fr (O.Z.); amor.mosbah@gmail.com (A.M.); ameur.cherif@uma.tn (A.C.)
[2] Department of Biology, Faculty of Sciences of Tunis, University of Tunis El Manar, Farhat Hachad Universitary Campus, Rommana 1068, Tunis, Tunisia
[3] Unit of hemodialysis, Military Training Hospital, Mont Fleury 1008, Tunis, Tunisia; bafounanis@gmail.com (A.B.)
[4]. Unit of organ transplantation, Military Training Hospital, Mont Fleury 1008, Tunis, Tunisia; imenelkosai@gmail.com (I.K.); Manaajamel@yahoo.fr (J.E.M.)
[5] Laboratory of Systems Microbiology and Applied Genomics, Department of Sustainable Agriculture, Uni-versity of Patras, 2 Seferi St, 30100 Agrinio, Greece; eliasasim@gmail.com (E.A.); panayotastathopou-lou@gmail.com (P.S.); gtsiamis@upatras.gr (G.T.)
* Correspondence: soumayakouidhi@gmail.com; Tel.: +216-29-810-100

Chronic kidney disease (CKD) and its complications are a growing global and African health burden. Emerging evidence highlights the gut microbiome's role in influencing disease progression, immune responses, and post-transplant outcomes. Over the last decade, our team at the laboratory of biotechnology and valorization of bio-geo resources, University of Manouba-Tunisia, was focused on the study of microbiome in health, CKD and kidney replacement among other pathologies. We conducted a series of case-control studies where we combined metagenomic and metabolomic approaches to explore gut microbial shifts and metabolic signatures in CKD patients undergoing hemodialysis and in stable kidney transplant recipients.

We recruited 40 kidney transplant patients (≥3 months post-transplant), 19 hemodialysis patients, and 18 healthy controls. Using 16S rRNA amplicon sequencing, we observed reduced gut microbial richness and diversity in both patient groups. In hemodialysis patients, increased abundance of butyrate-producing bacteria (e.g., Lachnospiraceae, Ruminococcaceae, Bifidobacterium) was associated with gender and treatment duration. In transplant recipients, enrichment in Escherichia-Shigella and Parabacteroides correlated with post-graft time and comorbidities.

Additionally, we developed a novel untargeted GC-MS workflow to distinguish metabolic profiles of transplant recipients from healthy individuals. Metabolomic changes pointed to alterations in fatty acid biosynthesis and amino acid metabolism, indicating potential biomarkers for clinical monitoring.

Our integrative microbiome-metabolome analysis offers promising tools for patient stratification and personalized care in kidney disease. These findings support the value of microbiome science in transforming kidney health across Africa and globally.

Keywords: microbiome, kidney disease, transplantation, metagenomics, metabolomics, Africa, dysbiosis, GC-MS