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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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Untargeted urinary metabolomics reveals novel biomarkers for type 2 diabetic kidney disease

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Objectives : Current availability of urine biomarkers for diabetic kidney disease (DKD) in the context of type 2 diabetes is limited, with albuminuria being the primary biomarker. Herein, untargeted urinary metabolomics was performed to identify novel metabolic biomarkers of DKD, particularly focusing on comparing urinary profiles with those of healthy individuals and diabetic patients without kidney involvement.
Methods : The study encompassed a cohort of 96 patients with biopsy-proven type 2 DKD patients from November 2011 to December 2022. Untargeted metabolomic analysis was applied to urine samples collected from these patients, utilizing a high-resolution liquid chromatography-tandem mass spectrometry system. Comparative analyses were conducted with two control groups: healthy individuals (n = 79) and type 2 diabetic patients without kidney involvement (n = 76). To account for variations in urinary dilution, the processed feature data underwent normalization using the probability quotient normalization method.
Results : The comparison between DKD and healthy individuals revealed alterations in 61 metabolites, with 27 upregulated and 34 downregulated. When contrasting DKD with diabetes without kidney involvement, 80 metabolites showed differences, including 31 upregulated and 49 downregulated. The pathway analysis utilizing the Kyoto Encyclopedia of Genes and Genomes (KEGG) database highlighted the notable upregulation of tyrosine metabolism in the urinary profiles of DKD. Specifically, 2-phenylacetamide exhibited a significant elevation in patients with DKD compared to both healthy individuals and diabetic controls without kidney involvement.
Conclusions : The study emphasizes the significance of tyrosine metabolism as a distinctive urine feature of type 2 DKD, with 2-phenylacetamide standing out as a notable candidate for a potential diagnostic and therapeutic target.

Figure_1.png

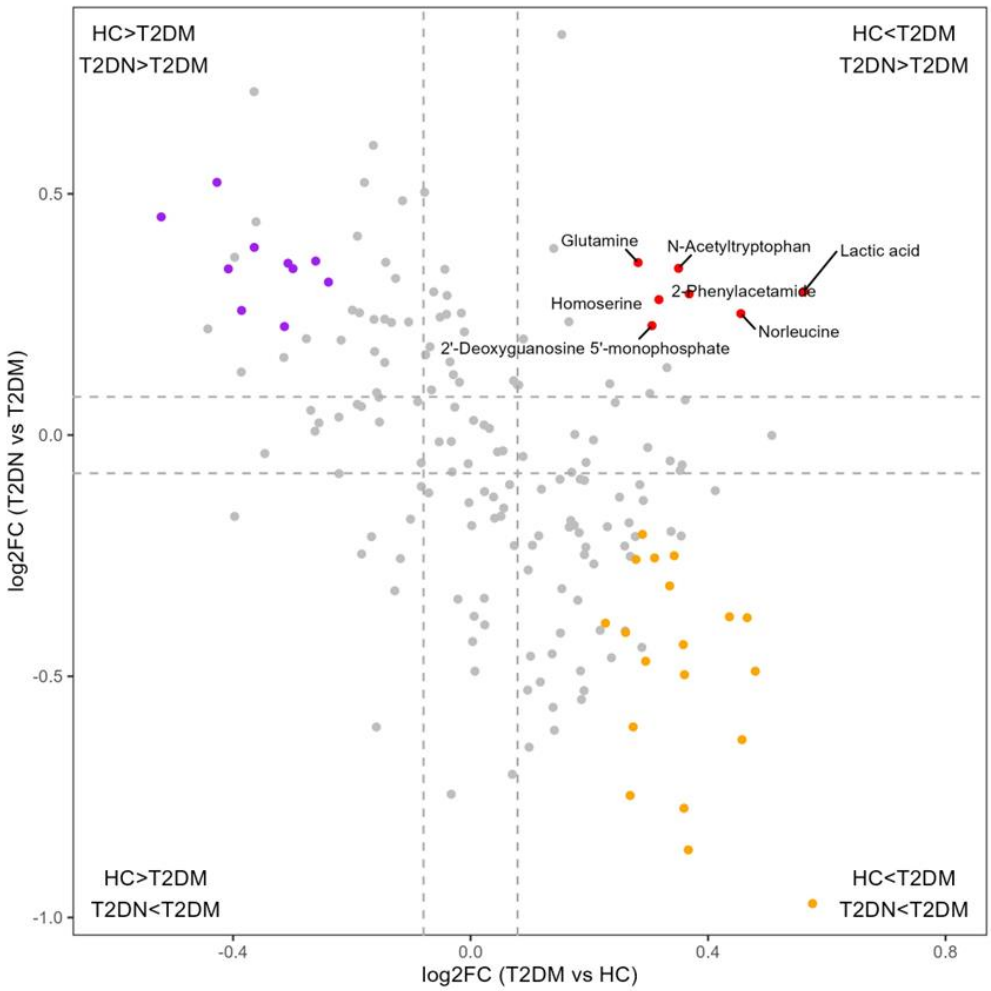
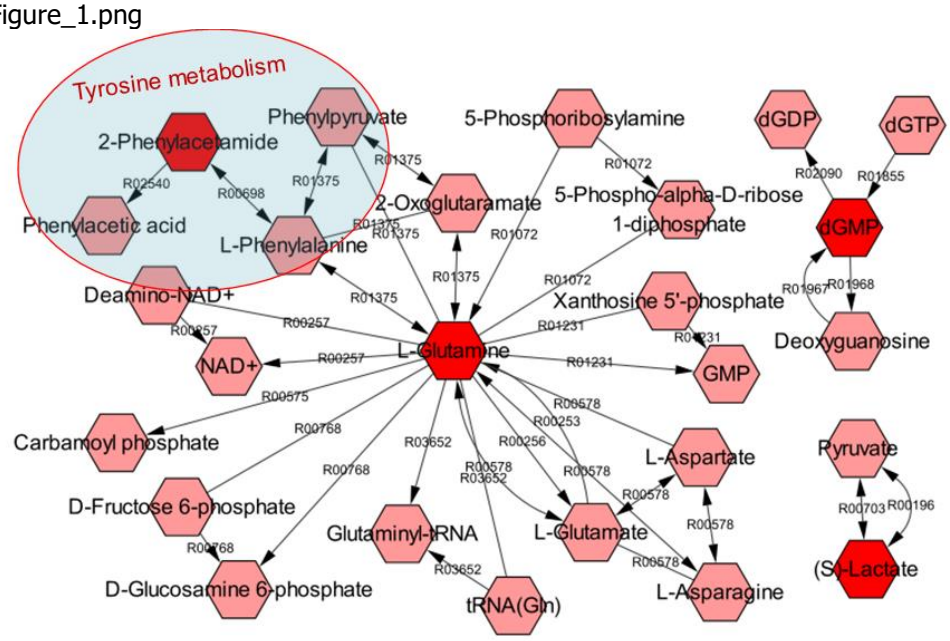

HC>T2DM
T2DN>T2DM
HC<T2DM
T2DN>T2DM
HC>T2DM
T2DN<T2DM
HC<T2DM
T2DN<T2DM
Glutamine
N-Acetyltryptophan
Lactic acid
2-Phenylacetamide
Homoserine
Norleucine
2'-Deoxyguanosine 5'-monophosphate
log2FC (T2DN vs T2DM)
log2FC (T2DM vs HC)
0.5
0.0
-0.5
-1.0
-0.4
0.0
0.4
0.8

Figure_1.png


Tyrosine metabolism
Phenylpyruvate
2-Phenylacetamide
Phenylacetic acid
L-Phenylalanine
2-Oxoglutaramate
5-Phosphoribosylamine
5-Phospho-alpha-D-ribose 1-diphosphate
dGDP
dGTP
dGMP
Deoxyguanosine
Deamino-NAD+
NAD+
L-Glutamine
Xanthosine 5'-phosphate
GMP
Carbamoyl phosphate
D-Fructose 6-phosphate
D-Glucosamine 6-phosphate
Glutaminyl-tRNA
tRNA(Gln)
L-Glutamate
L-Aspartate
L-Asparagine
Pyruvate
(S)-Lactate
R01375
R02540
R00698
R01072
R02090
R01855
R01967
R01968
R00257
R01231
R00575
R00768
R03652
R00253
R00256
R00578
R00703
R00196