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Causal effect of gut microbiota and diabetic nephropathy: a Mendelian randomization study

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Objectives : The interaction of gut microbiota (GM) with diabetes nephropathy (DN) drew our attention and a better understanding of GM on DN provided potential therapeutic approaches. However, the causal effect of GM on DN remains unknown.

Methods : We applied two-sample Mendelian Randomization (MR) analysis to screen the significant bacterial taxa based on the GWAS data. Sensitivity analysis was conducted to assess the robustness of MR results. To identify the most critical factor on DN, Mendelian randomization-Bayesian model averaging (MR-BMA) method was utilized. Whether the reverse causality existed was verified by reverse MR analysis. Finally, transcriptome MR analysis was performed to investigate the mechanism of GM on DN.

Results : We found eight taxa significantly related to DN. Among these taxa, genus Ruminococcus gauvreauii played a crucial role in DN. No causal relationship was identified between DN and GM in the reverse MR analysis. Furthermore, mapped genes FCGR2B and VNN2 might be the therapeutic targets for GM on DN.

Conclusions : This work provided new evidence for the causal effect of GM on DN and potential biomarkers for DN. The significant bacterial taxa in our study provided new insights for the 'gut-kidney' axis, as well as unconventional prevention and treatment strategies for DN.

Figure 3.png

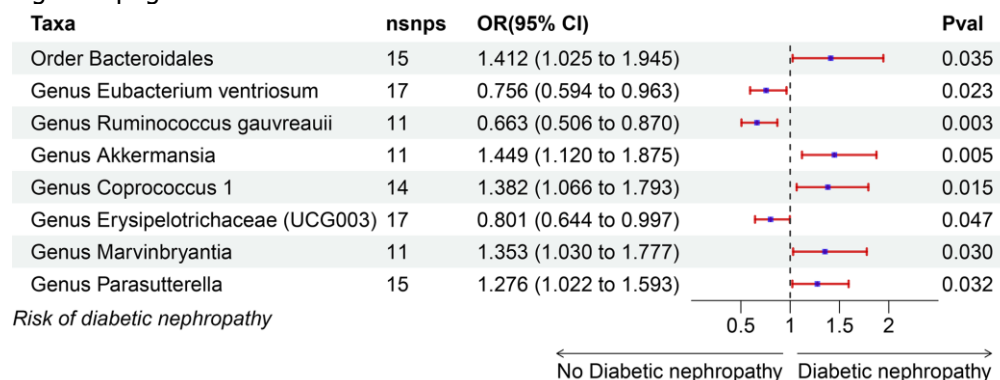


Figure 3.png

Mapping gene	nsnps	OR(95% CI)	Pval	FDR
Genus Ruminococcus gauvreauii				
APC	6	0.663 (0.458 to 0.959)	0.029	0.035
FCGR2B	76	0.943 (0.900 to 0.988)	0.014	0.023
FCRLB	41	0.846 (0.767 to 0.934)	<0.001	0.004
REEP5	50	0.890 (0.818 to 0.968)	0.006	0.016
SDHC	17	1.067 (1.001 to 1.137)	0.047	0.047
TCEB2	11	0.773 (0.665 to 0.898)	<0.001	0.004
Genus Marvinbryantia				
CRY2	32	1.108 (1.016 to 1.209)	0.020	0.028
NDRG2	16	0.809 (0.661 to 0.989)	0.039	0.040
VNN1	101	0.957 (0.924 to 0.992)	0.016	0.025
VNN2	78	1.063 (1.017 to 1.110)	0.006	0.017
VNN3	98	1.062 (1.010 to 1.117)	0.018	0.026

Risk of diabetic nephropathy

