



Intestinal microbiota by angiotensin receptor blocker therapy exerts protective effects against hypertensive damages.

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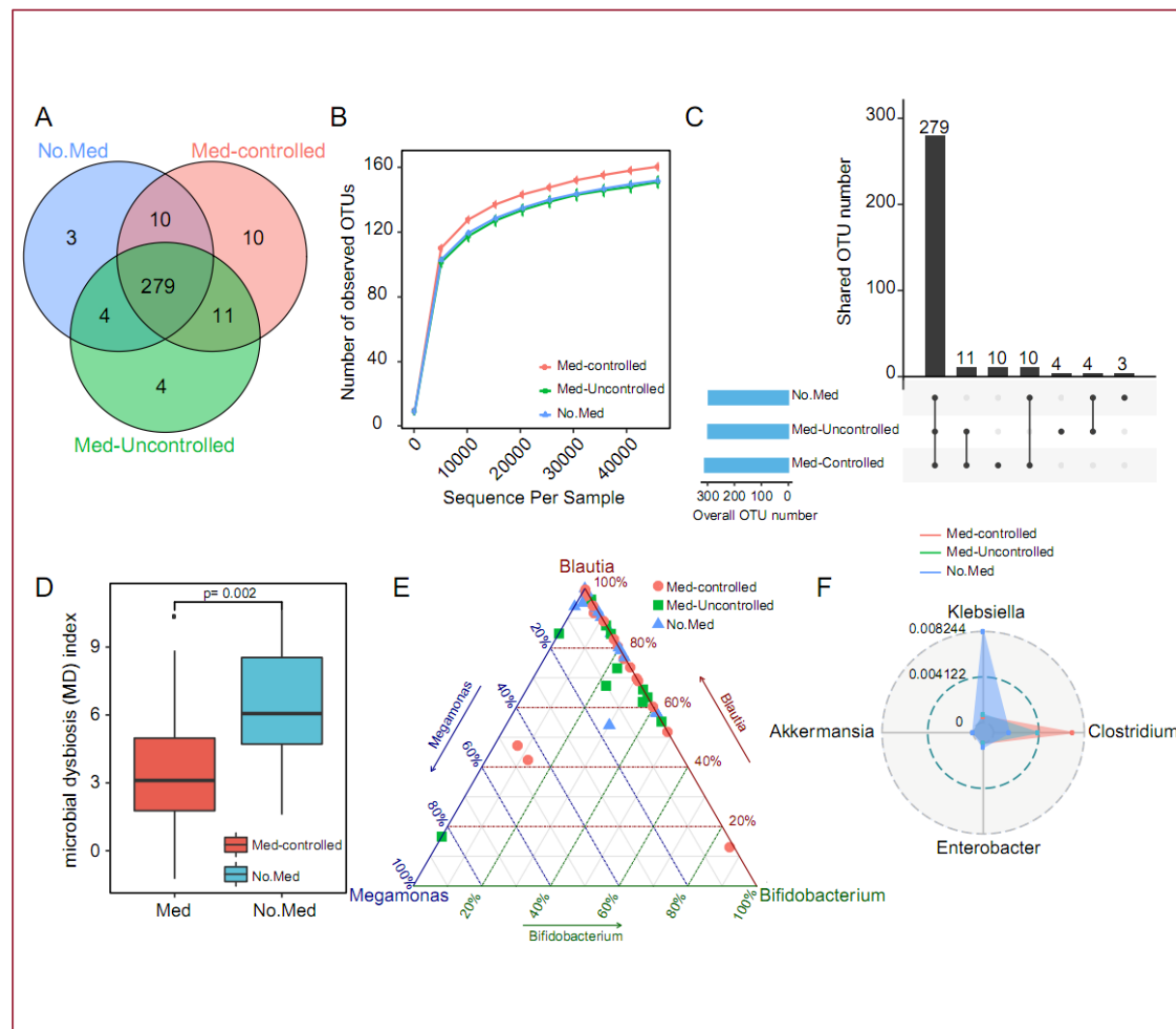
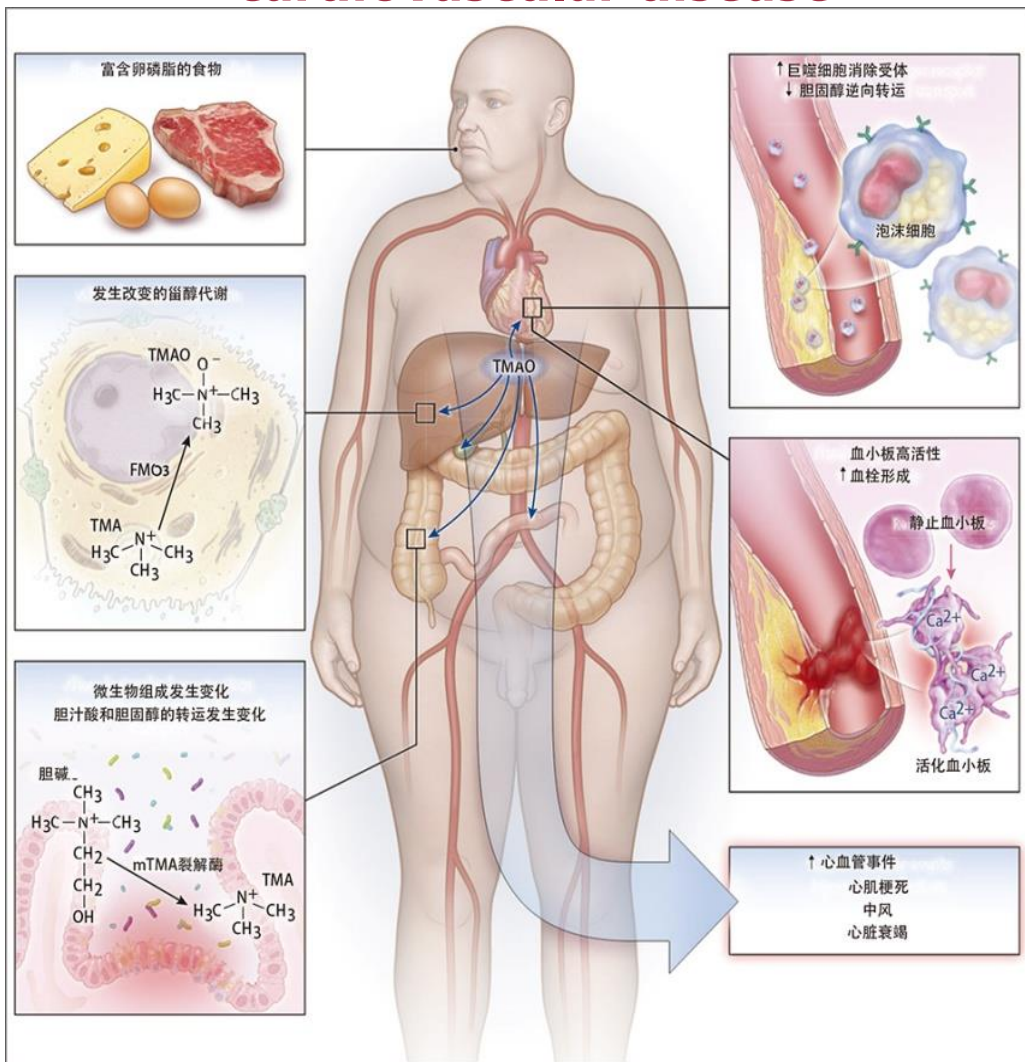


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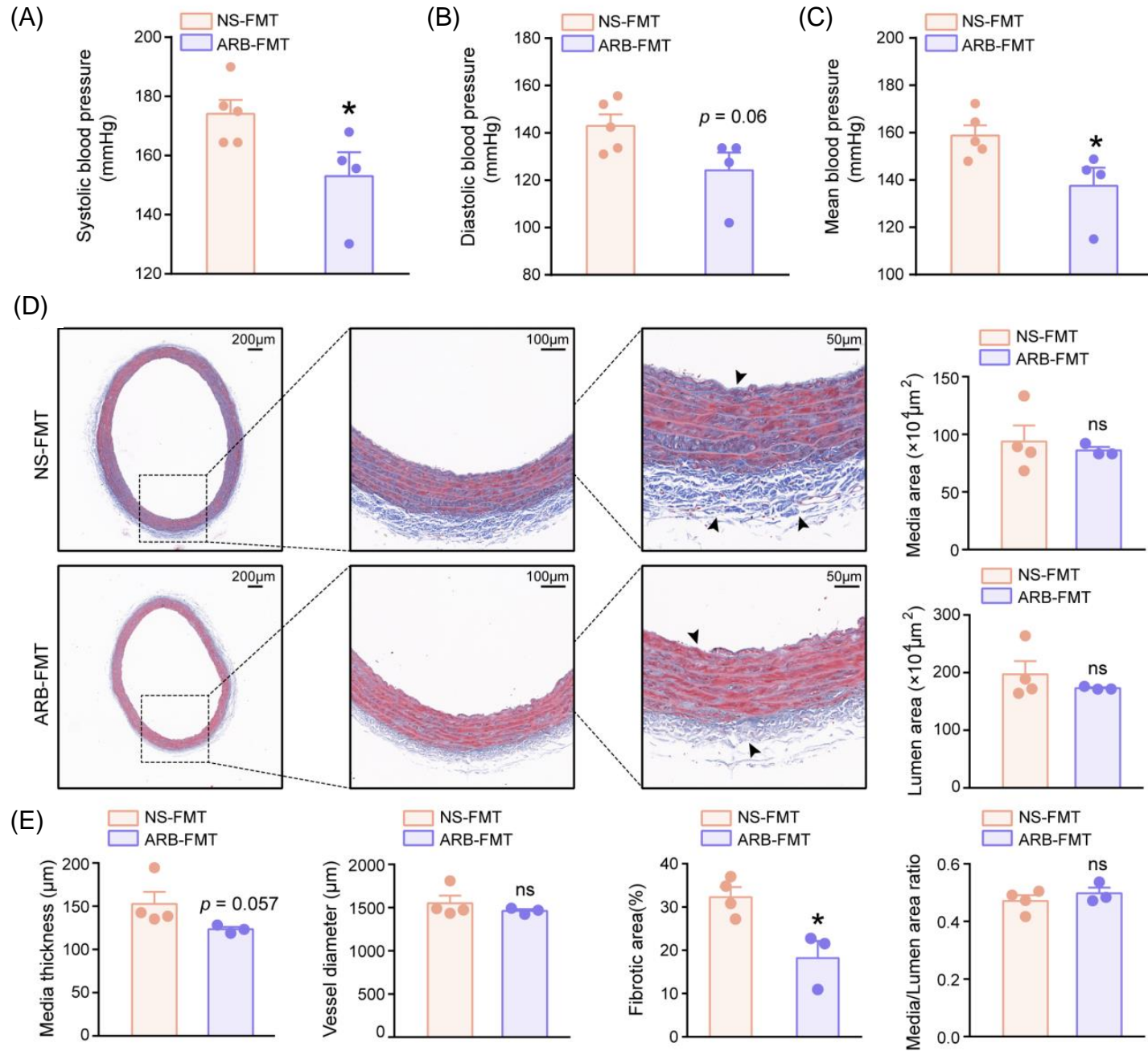
Introduction

Intestinal microbiota is closely linked to cardiovascular disease



Manipulation of the gut microbiota in hypertensive patients treated with ACEI/ARB

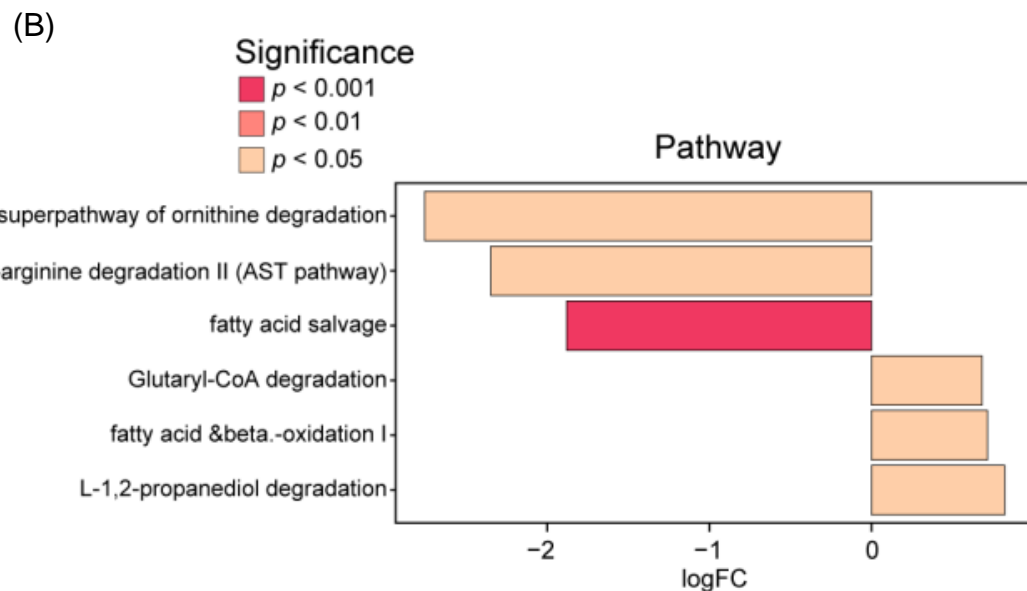
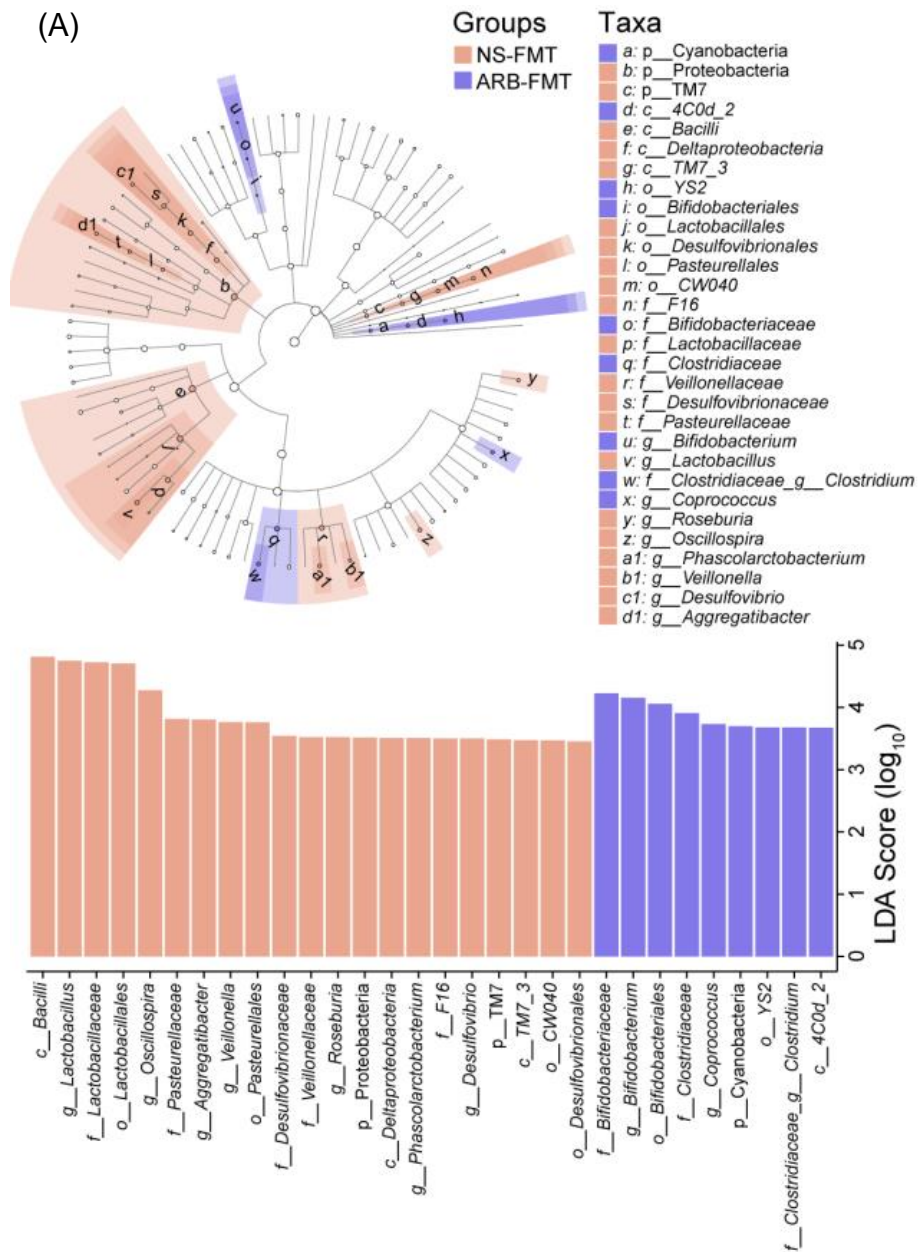
ARB-modulated gut microbes ameliorate high BP and vascular damage



- The blood pressure of SHR rats significantly decreased after ARB-FMT.
- ARB-FMT visibly reduced vascular fibrosis, but did not reverse vascular media thickness and media/lumen area ratio in hypertension.



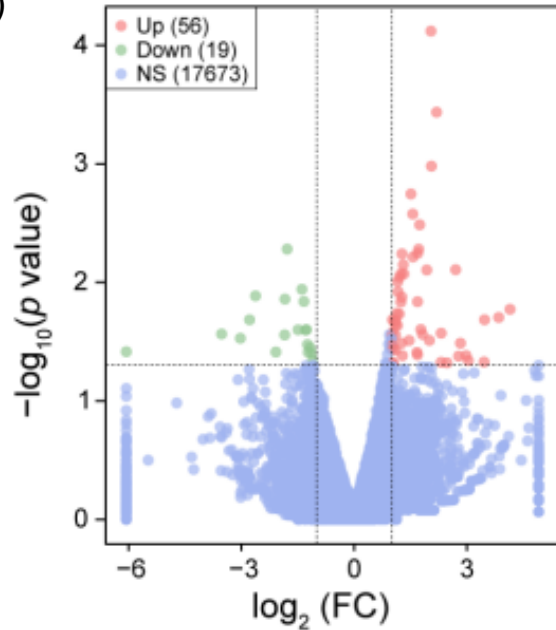
ARB-FMT rebuilds gut microbiota and affects intestinal gene profiles



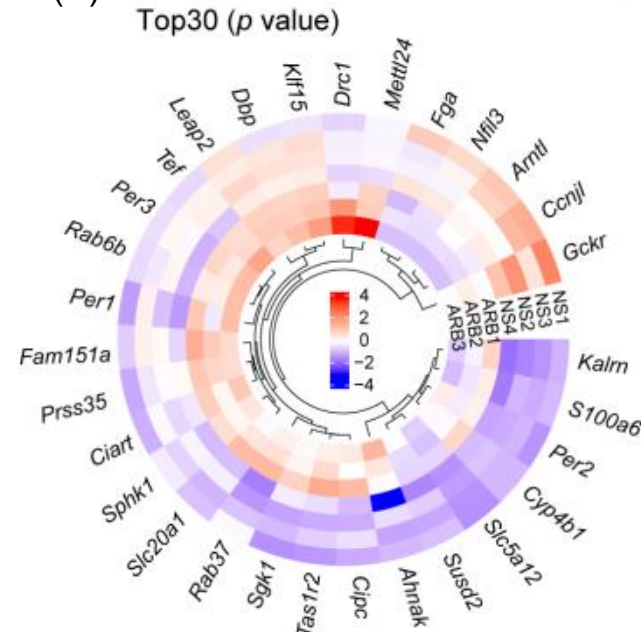
- *Bifidobacterium*, *Coprococcus*, and *Clostridium* were prominently elevated in SHRs receiving ARB-modified microbiota, while *Lactobacillus*, *Oscillospira*, *Aggregatibacter*, *Veillonella*, *Roseburia*, *Phascolarctobacterium*, *Desulfovibrio* were notably reduced.
- The capacities of the gut microbiota following ARB-FMT were significantly enhanced in pathways of Glutaryl-CoA degradation, fatty acid beta-oxidation, and L-1,2-propanediol degradation but decreased in L-arginine degradation, fatty acid salvage, and ornithine degradation.

Transcriptome and RNA expression profiles within the intestine of ARB-FMT rats

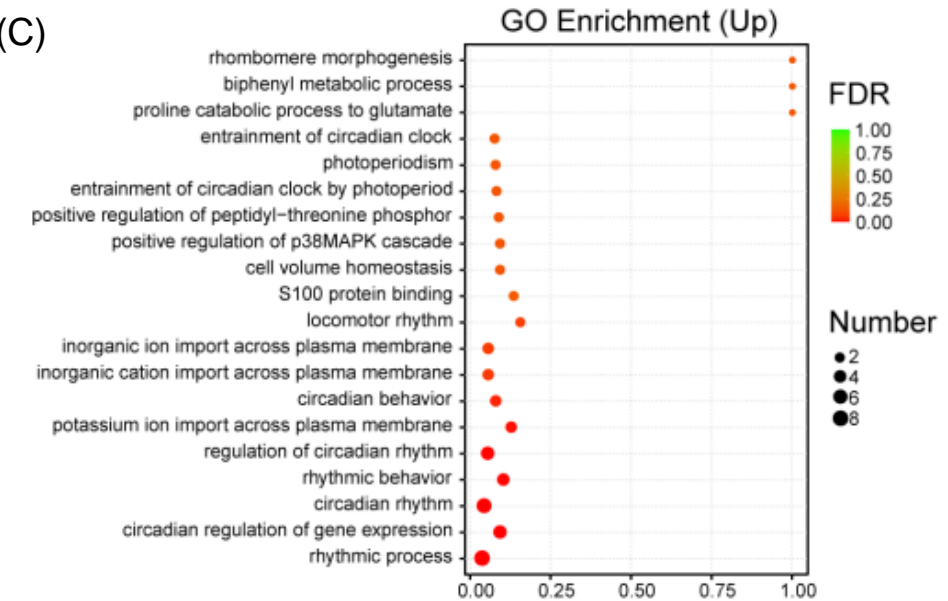
(A)



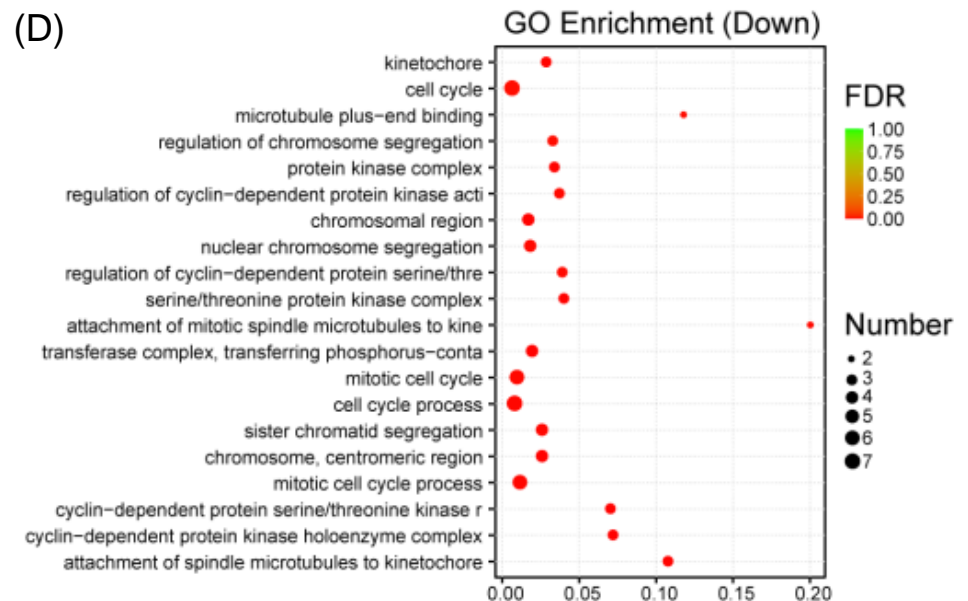
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(C)



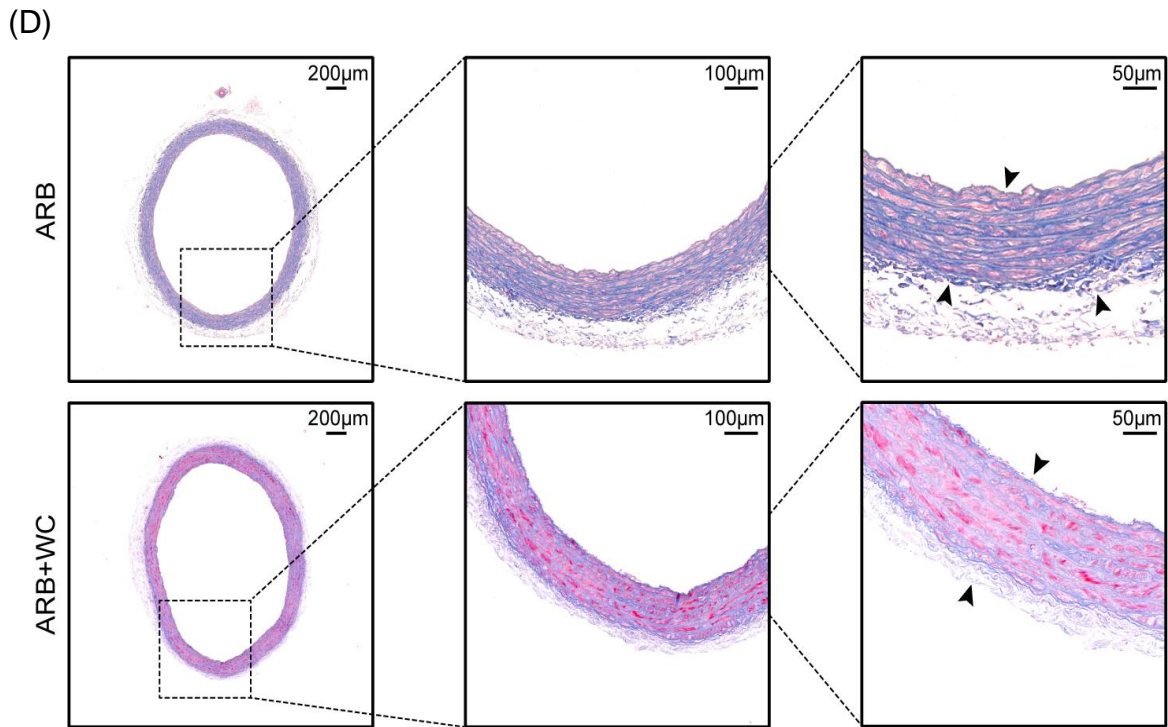
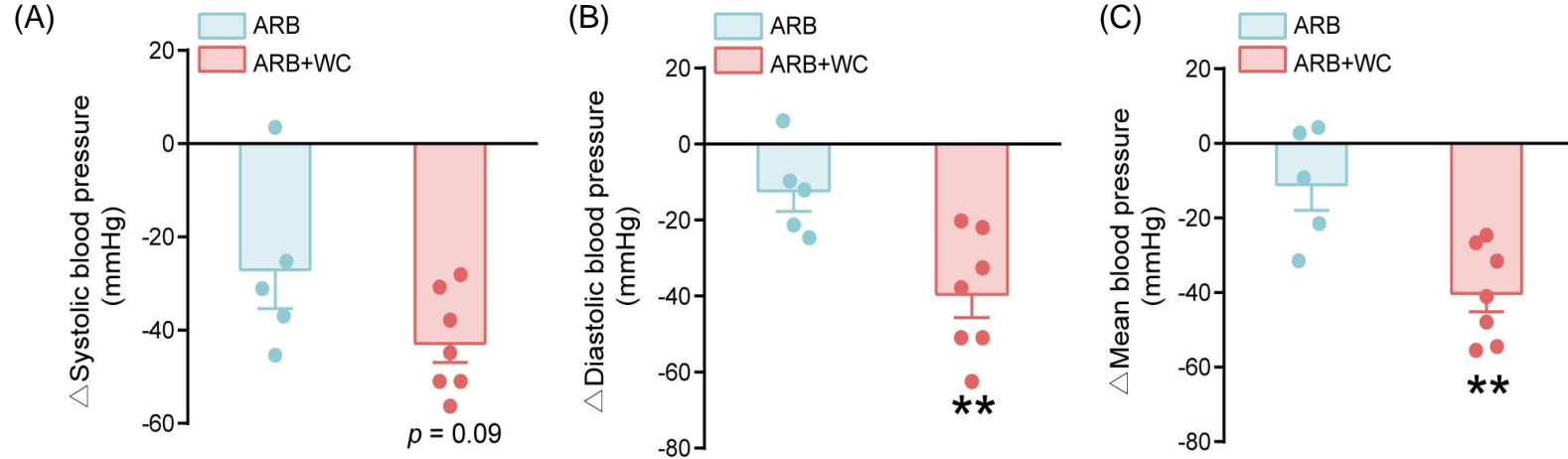
(D)



- ARB-FMT treatment significantly augmented the expression of 56 genes and abated the expression of 19 genes in the gut.
- The reduction of *Nfil3* and *Arntl*, as well as the upregulation of *Ciart*, *Cipc*, *Per1*, *Per2*, *Per3*, *Tef*, *Sgk1*, *Dbp*, *Pdk4*, *Klf15* etc., were consistently observed after ARB-FMT.
- GO enrichment analysis indicated remarkably enhanced potentials of circadian rhythm in ARB-FMT rats but deficient abilities to constitute cyclin-dependent protein serine/threonine kinase and protein kinase holoenzyme complex.

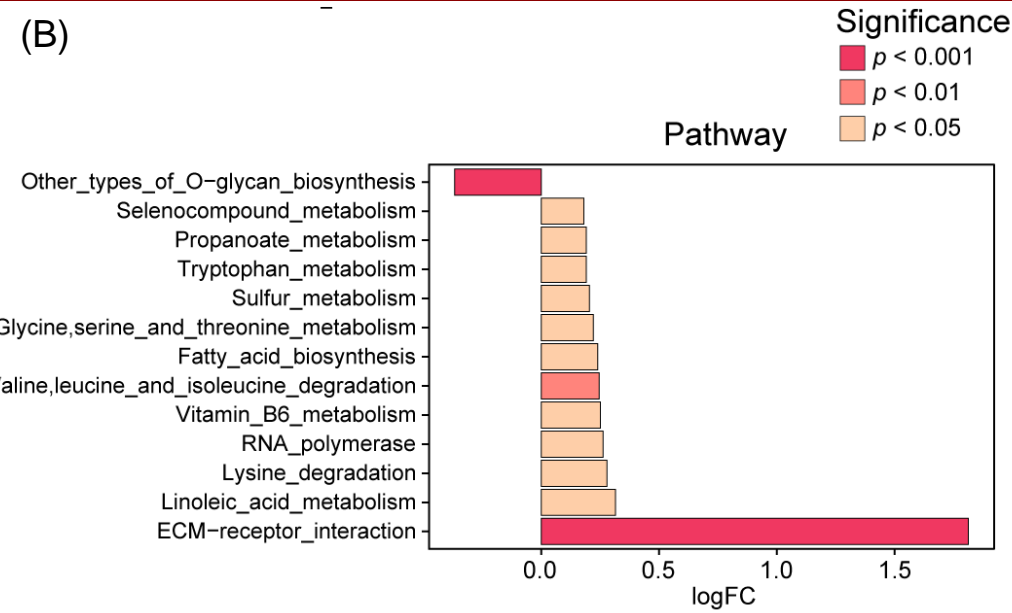
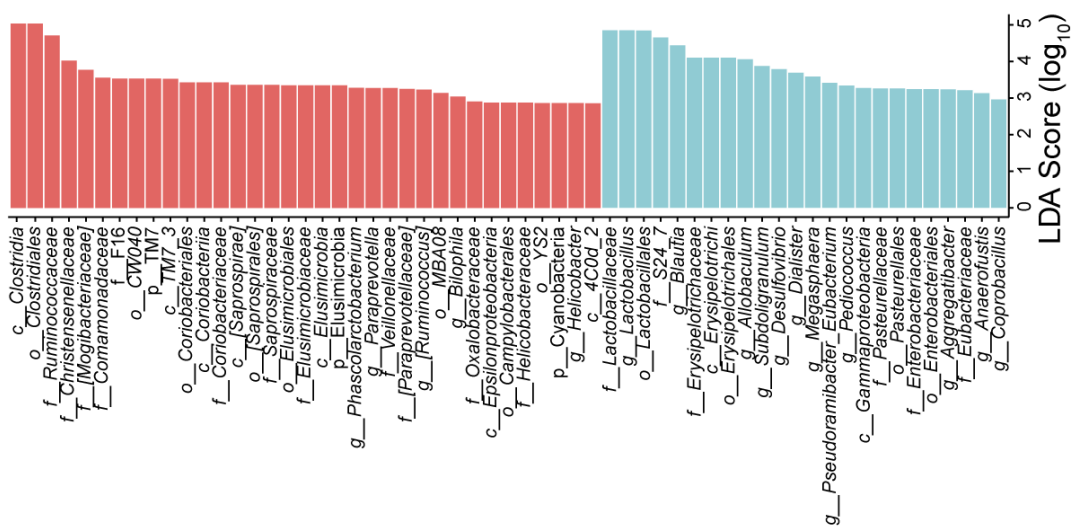
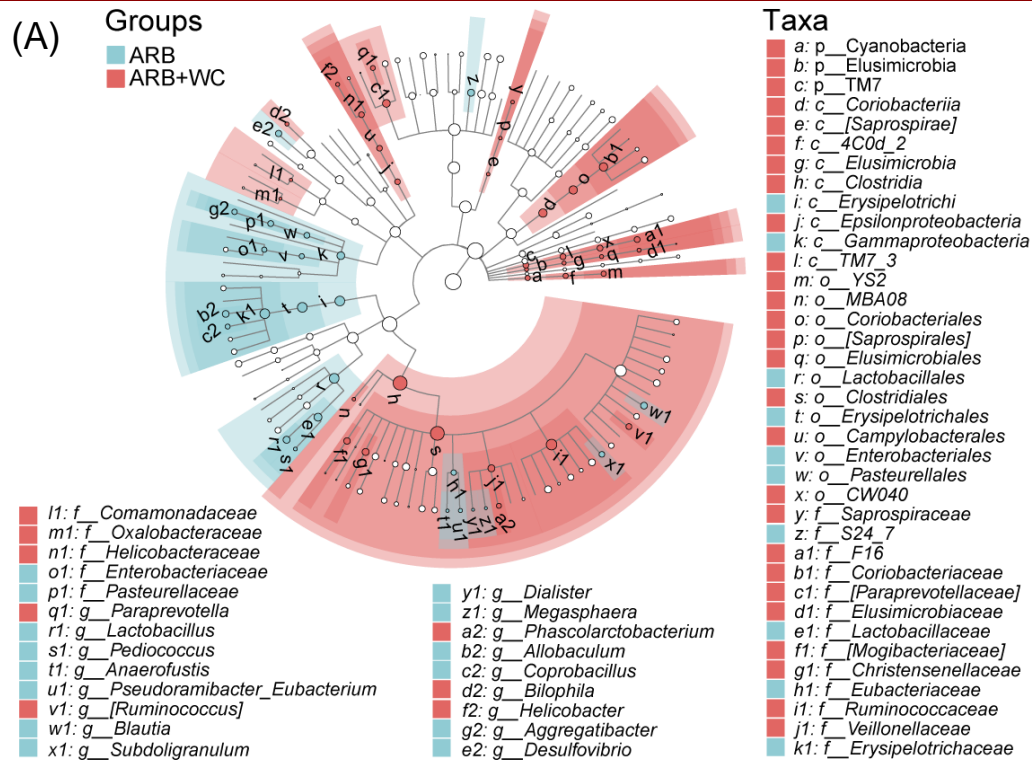


WC-FMT improved the therapeutic efficacy of valsartan in SHRs.



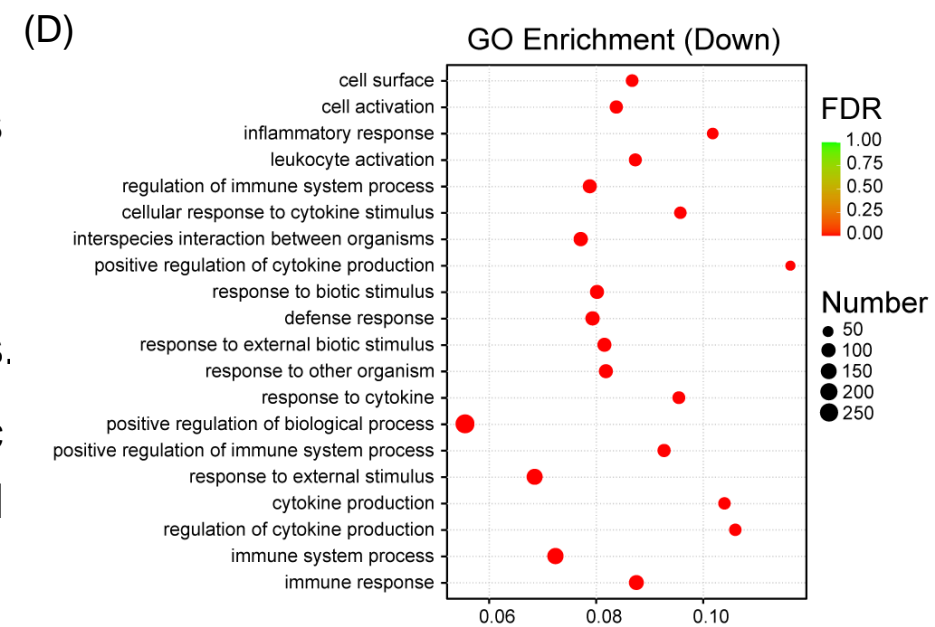
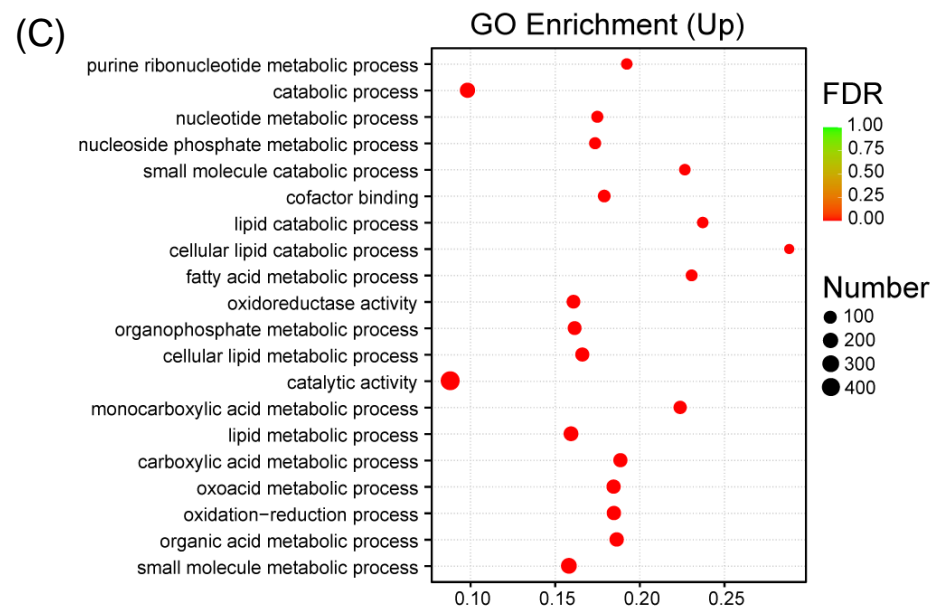
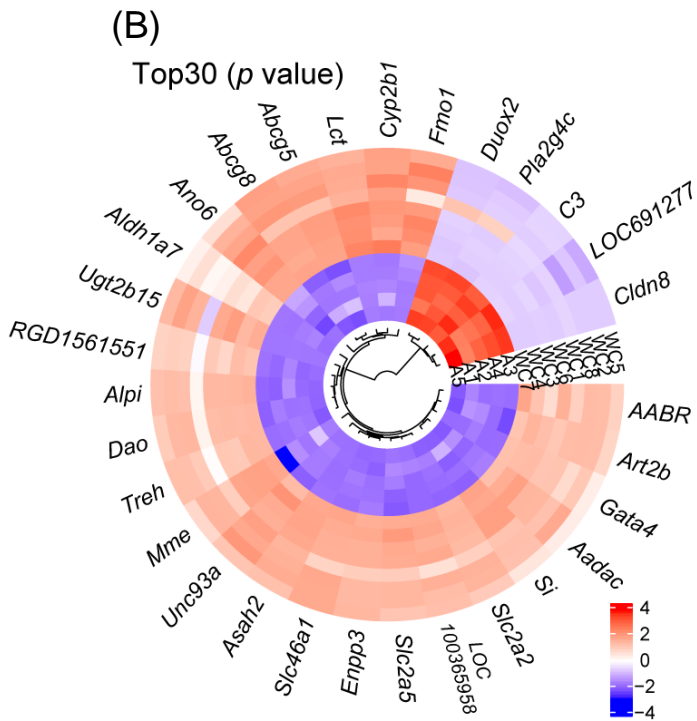
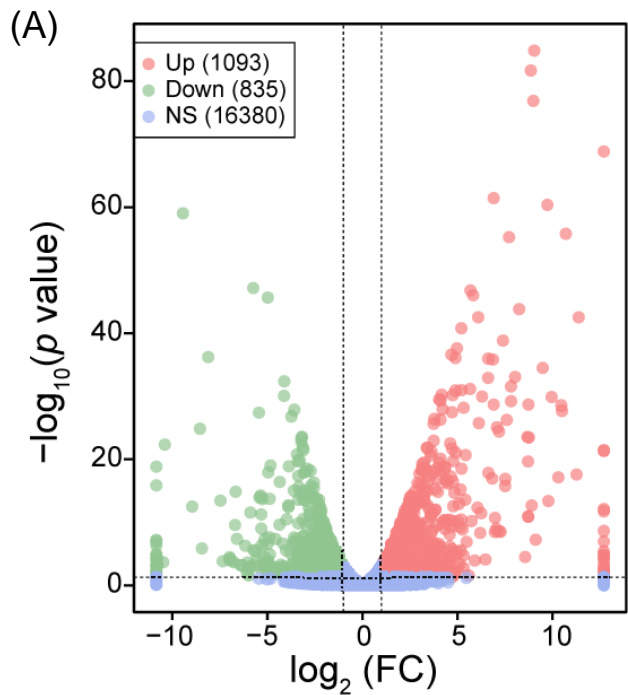
- The gut microbiota of WC hypertensive patients improved the antihypertensive effect of valsartan.
- WC-FMT remarkably enhanced the effect in ARB reducing vascular fibrosis.

Manipulation of the gut microbiota by supplementing bacteria from WC donors



- Microbes markedly enriched in FMT plus ARB-treated animals were *Phascolarctobacterium*, *Paraprevotella*, *Bilophila*, and *Helicobacter*, whereas the depleted bacteria included *Pediococcus*, *Megasphaera*, *Dialister*, *Aggregatibacter*, *Coprobacillus*, *Lactobacillus*, *Desulfovibrio*, etc.
- WC-FMT has an impact on the gut microbiota function of ARB intervention in SHR rats, promoting the metabolism of linoleic acid and tryptophan, the degradation of valine, leucine, and isoleucine but suppressed O-glycan.

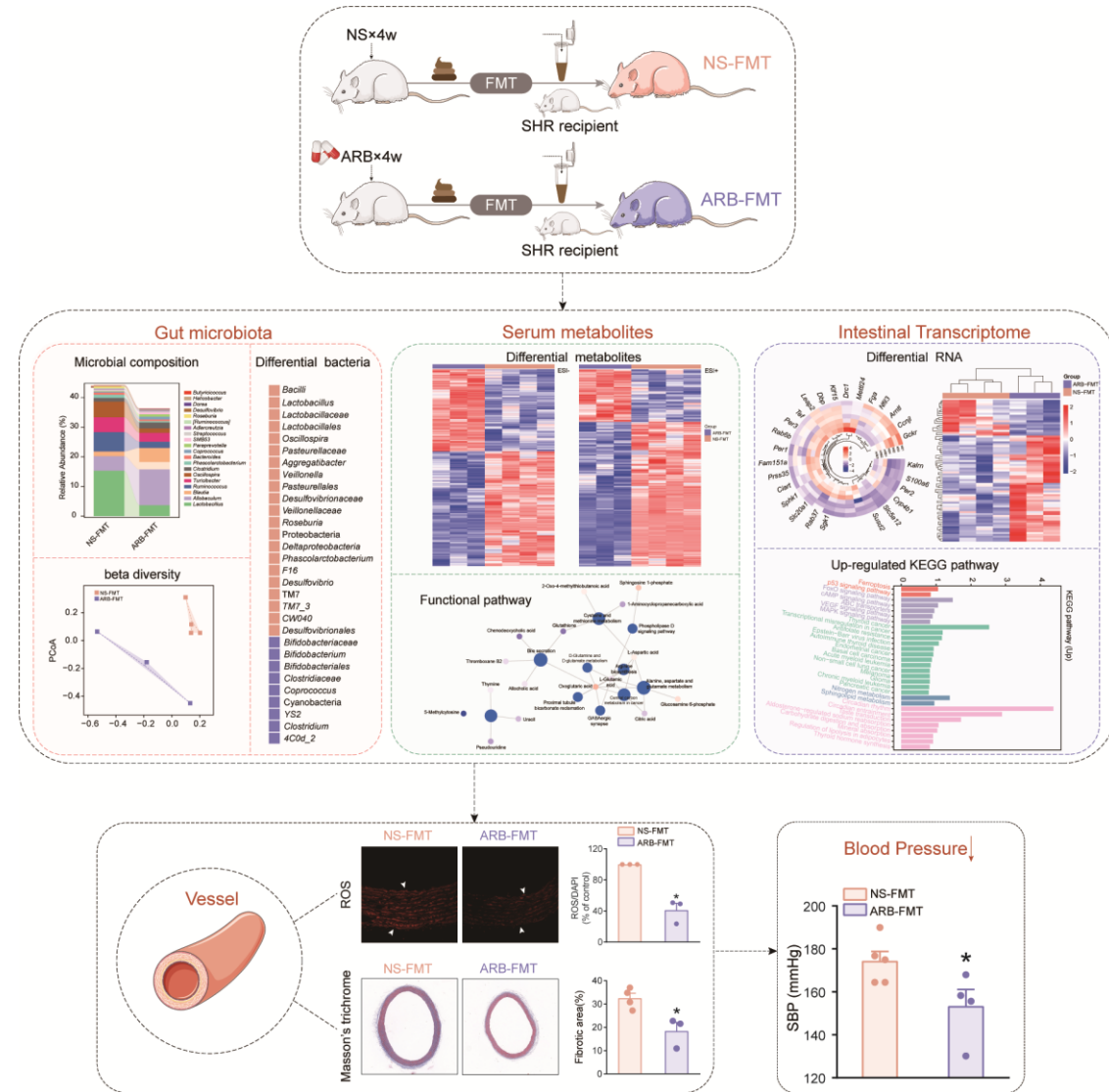
Transcriptome profiles of RNA in the intestine are affected by WC microbiota



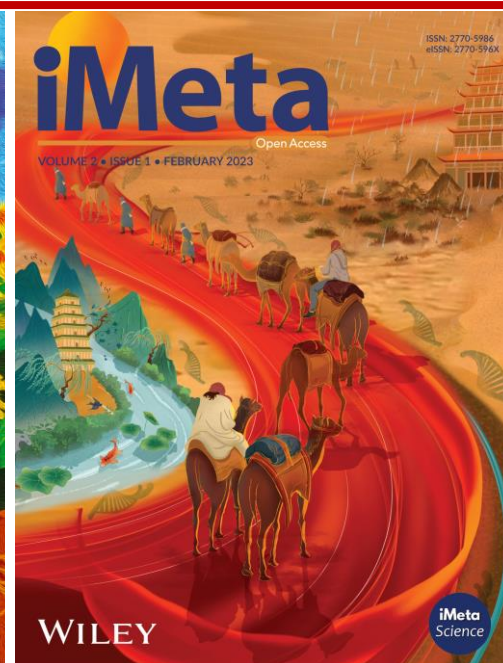
- In the ARB+WC group, 1,093 dramatically increased, and 835 genes decreased.
- The reduction of *Duox2*, as well as the upregulation of *Asah2*, *Lct*, *Alpi*, *Si*, *Aadac*, *Dao* etc., were affected by WC microbiota in ARB rats.
- The genes enhanced in ARB+WC were implicated in monocarboxylic acid, fatty acid metabolism, and lipid catabolism, while those depleted had a crucial role in the immune system and inflammatory response.

Summary

- Angiotensin receptor blocker (ARB)-modified gut microbiota lead to reduced systolic blood pressure (BP) levels and exert protective roles in spontaneously hypertensive rats (SHRs).
- ARB-modified fecal microbiota transplantation (FMT) contributes to the reconstruction of the gut microbiota, serum metabolome and intestinal transcriptome in SHRs.
- Fecal microbiota from hypertensive patients treated with ARB improved the therapeutic efficacy of valsartan in SHRs.




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