Alterations in gut microbiota and metabolites associated with altitude-induced cardiac hypertrophy in rats

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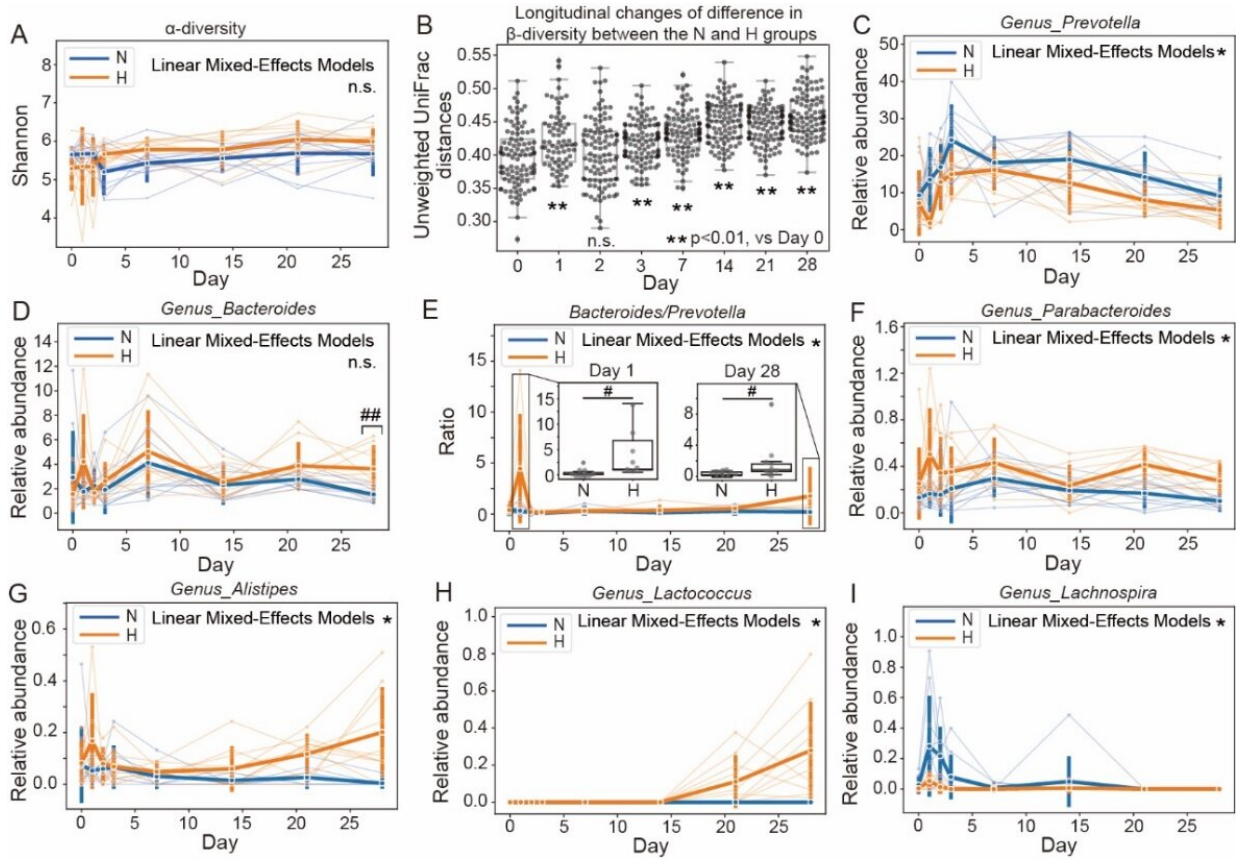


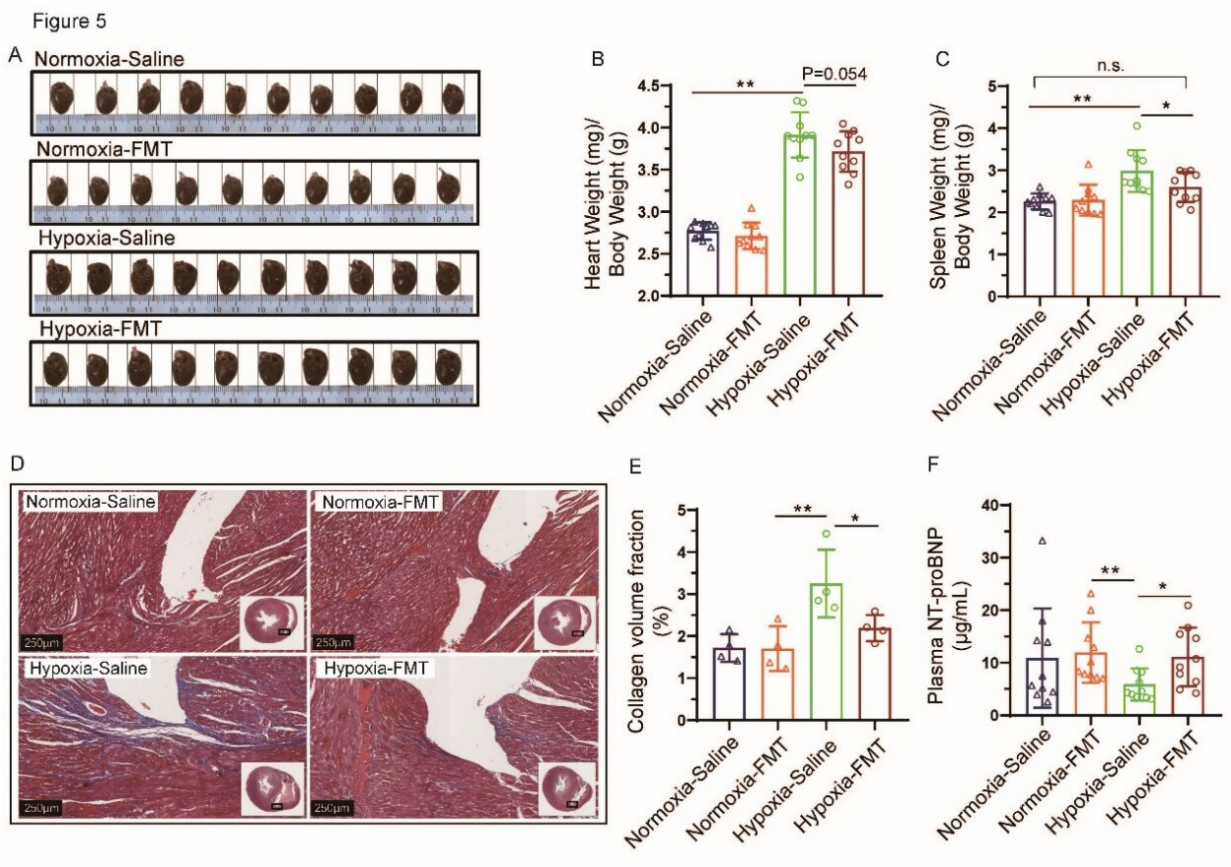
The Prevotella genus was sharply decreased in the challenged rats, especially on day 1. In contrast, the abundance of the Bacteroides genus was slightly increased, leading to a higher Bacteroides to Prevotella ratio in the model rats, particularly on day 1 and day 28. The abundance of the Parabacteroides and Aplistipes genera was increased on day 1 after hypoxic stimuli, with a small decrease later, but was maintained at a higher level than that in the control group at all the

sampling time points. Meanwhile, the abundance of the Lactococcus genus began to increase 2 weeks post the hypobaric hypoxia challenge. In contrast, the Lachnospira genus was suppressed in the acute period after the hypobaric hypoxia challenge. Credit: Science China Press

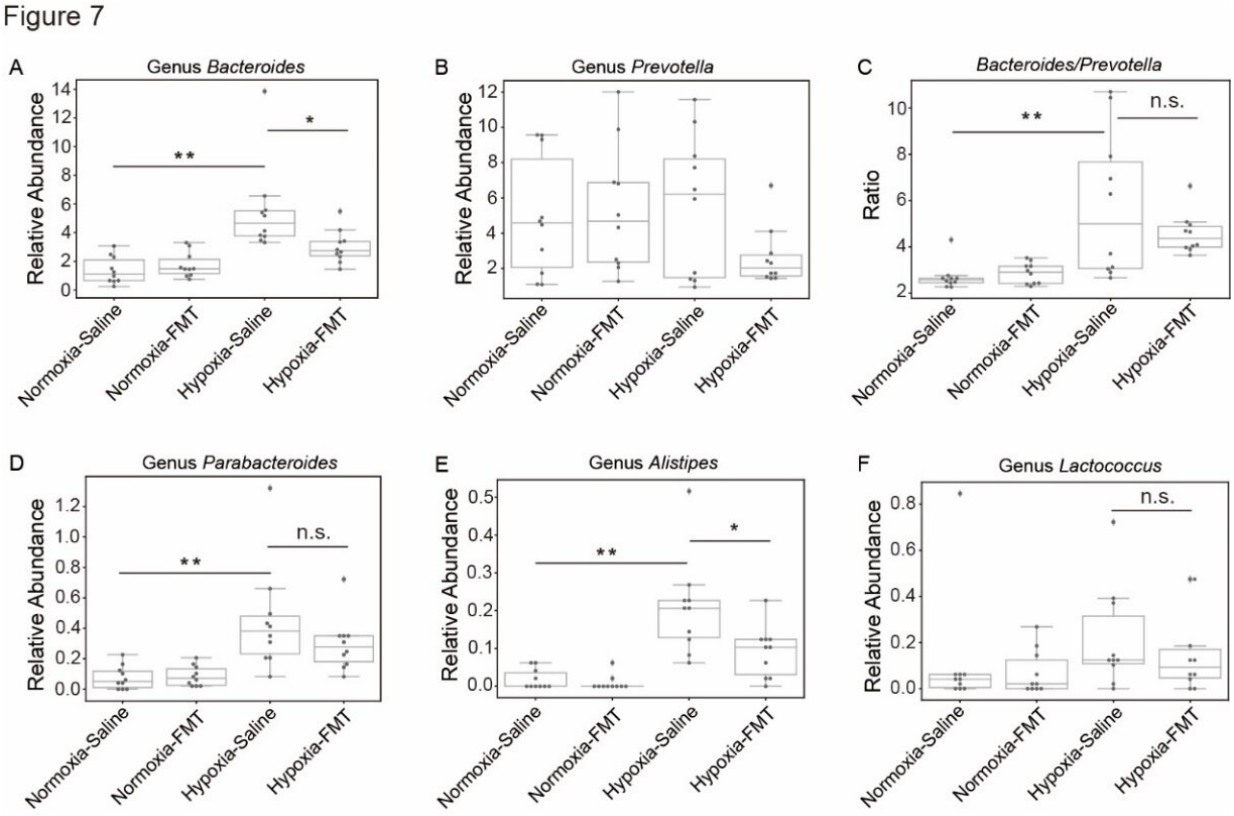
Accumulating evidence has shown that there are great differences in the structure and diversity of intestinal microorganisms in mammals or humans living at different altitudes. However, it is still unknown whether such changes play a role in the development and progression of chronic altitude-related diseases, especially in high-altitude heart disease.

Therefore, researchers led by Dr. Ruifu Yang first developed a rat model of high-altitude heart disease by exposing the rats in a hypobaric chamber, simulating the altitude of 5,000 meters for 28 days. Then, they used 16S rDNA amplicon sequencing combined with targeted metabonomics to monitor the dynamics of intestinal microbes and their metabolites during this process. They identified that the hypobaric hypoxia-induced pathological cardiac hypertrophy in rats was accompanied by a large compositional shift in the gut microbiota, which was characterized by increased abundances of the Parabacteroides, Alistipes, and Lactococcus genera and a larger Bacteroides to Prevotella ratio.

Trans-omics analyses showed that the gut microbiome was significantly correlated with the metabolic abnormalities of short-chain fatty acids and bile acids in feces, suggesting an interaction network remodeling of the microbiome-metabolome after the hypobaric hypoxia challenge. Interestingly, the transplantation of fecal microbiota (FMT) ameliorated the pathological cardiac hypertrophy and fibrosis in hypoxic rats, which was due to an inhibition of the Bacteroides and Alistipes genera abundances after FMT treatment.



The FMT treatment moderately attenuated cardiac hypertrophy and spleen index in hypoxic rats, alleviated the severity of collagen deposition which was expressed as a collagen volume fraction. Credit: Science China Press



At the genus level, FMT treatment significantly inhibited the increase in the abundance of the Bacteroides and Alistipes genera, moderately suppressed the increase in the abundance of Parabacteroides and Lactococcus and the ratio of Bacteroides/Prevotella. Credit: Science China Press

In addition, they also demonstrated that administrations of probiotics, prebiotics, and synbiotics could significantly alleviate high-altitude heart disease in the same model.

Taken together, this study provides an insight into the longitudinal changes in intestinal microecology during the hypobaric hypoxia challenge, suggesting a promising strategy to prevent or treat high-altitude heart disease through regulating the gut microbiota.

The research was published in *Science China Life Sciences* and *Microbiology Spectrum*.

More information: Zhiyuan Pan et al, Alterations in gut microbiota and metabolites associated with altitude-induced cardiac hypertrophy in rats during hypobaric hypoxia challenge, *Science China Life Sciences* (2022). DOI: 10.1007/s11427-021-2056-1

Yichen Hu et al, Gut Microbiome-Targeted Modulations Regulate Metabolic Profiles and Alleviate Altitude-Related Cardiac Hypertrophy in Rats, *Microbiology Spectrum* (2022). DOI: 10.1128/spectrum.01053-21

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