

Chondroitin sulfate restores muscle mass via gut–muscle axis remodeling through sugar–bile acid metabolism reprogramming

Ruiyun Wu¹, Tao Wen², Nan Shang³, Penghao Xie²,
Zhenyu Wang¹, Hang Li⁴, Shaobo Li¹, Dequan Zhang¹

¹Institute of Food Science and Technology, Chinese Academy of
Agricultural Sciences, Beijing, China

²Jiangsu Provincial Key Lab for Organic Solid Waste Utilization, Nanjing Agricultural
University, Nanjing, China

³Collage of Engineering, China Agricultural University, Beijing, China

⁴Key Laboratory of Biomaterials of Guangdong Higher Education Institutes, Jinan University, Guangzhou, China



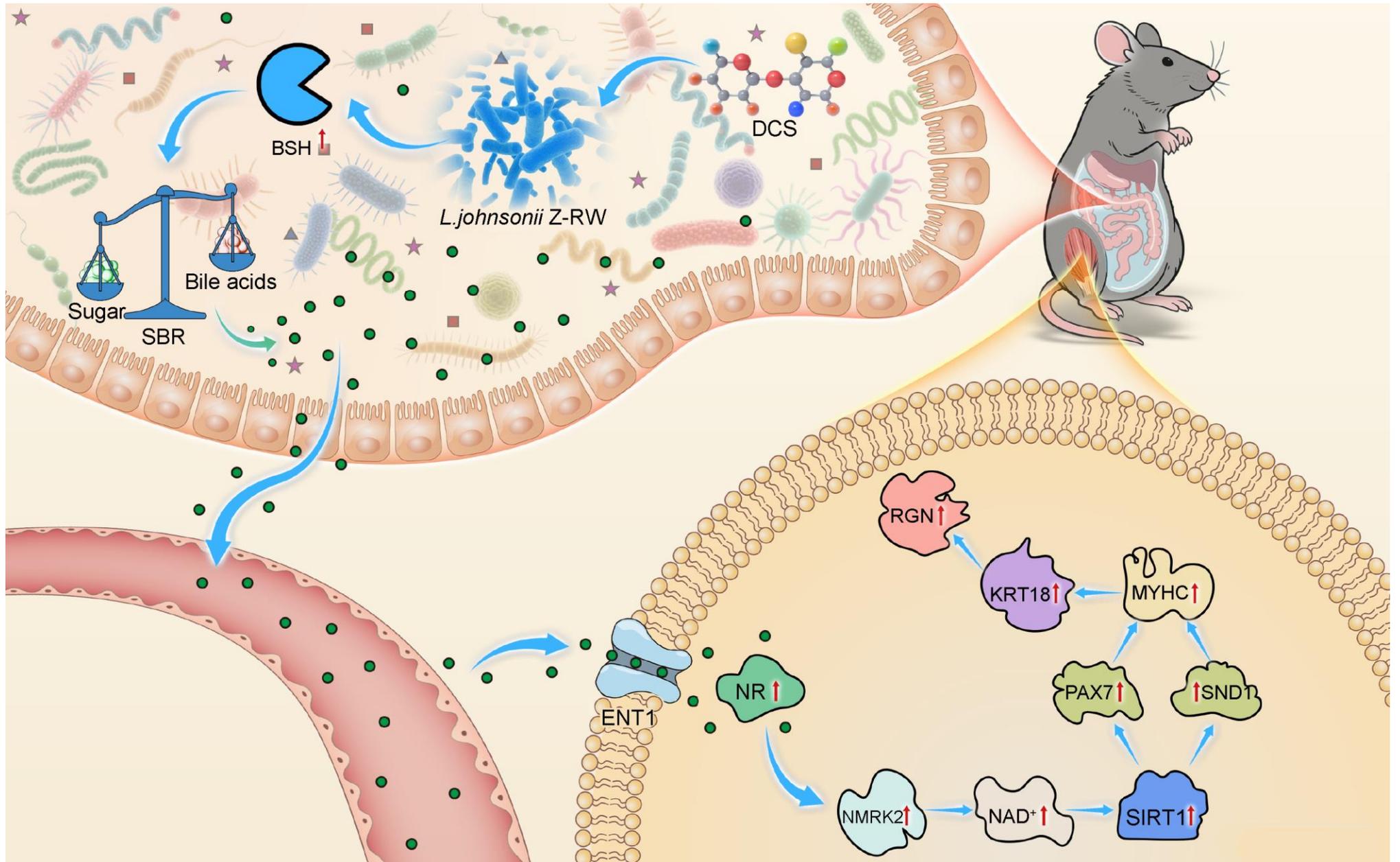
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Abstract

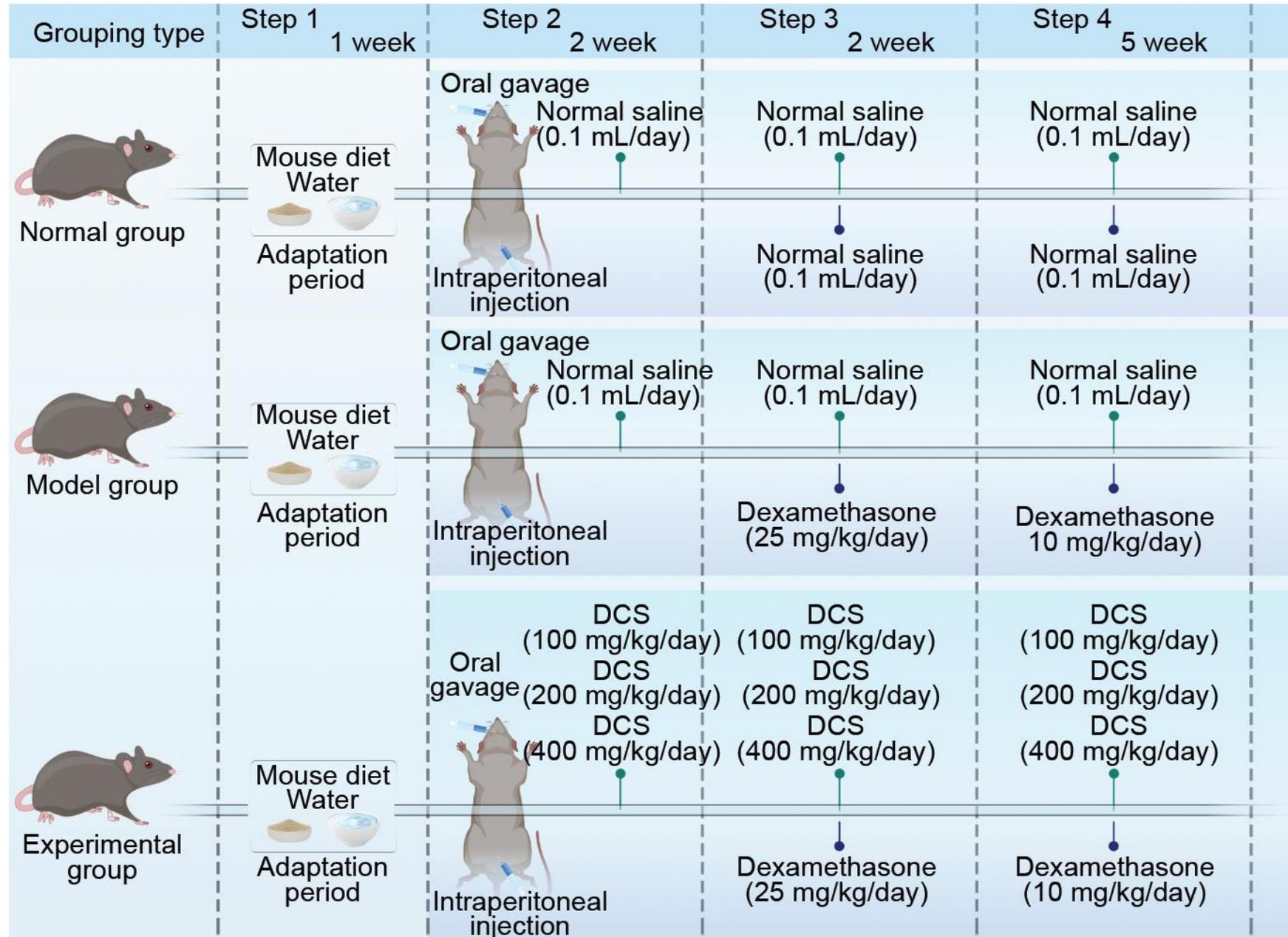
Graphical Abstract





Experimental design

Experimental Design and Flowchart



Main result— chondroitin sulfate improves muscle function

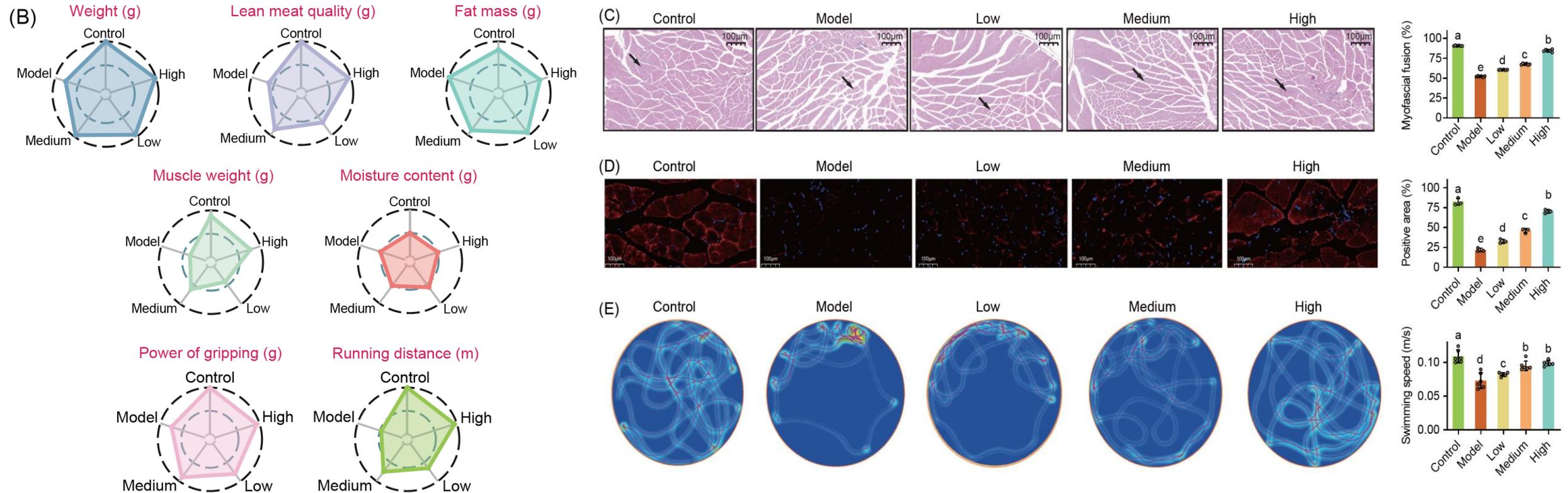


Figure 1. DCS enhances muscle regeneration and functional performance through remodeling of protein expression networks in myopathic mice.

Main result—chondroitin sulfate reshapes muscle proteome

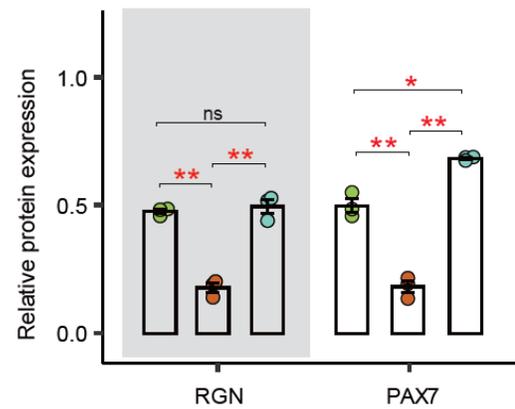
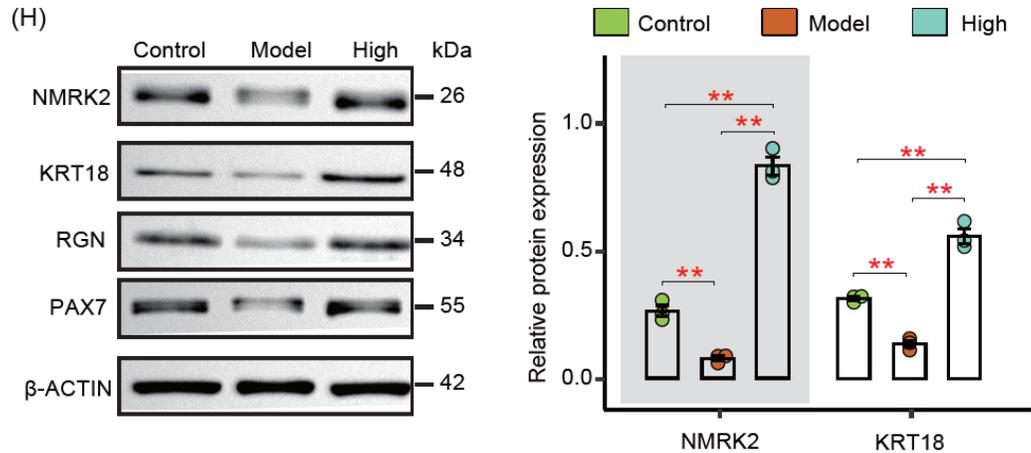
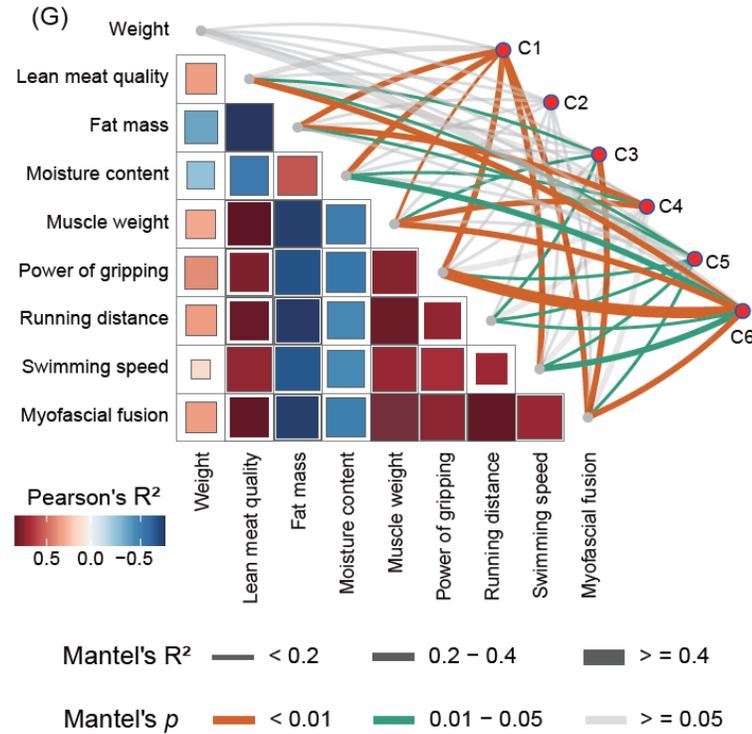
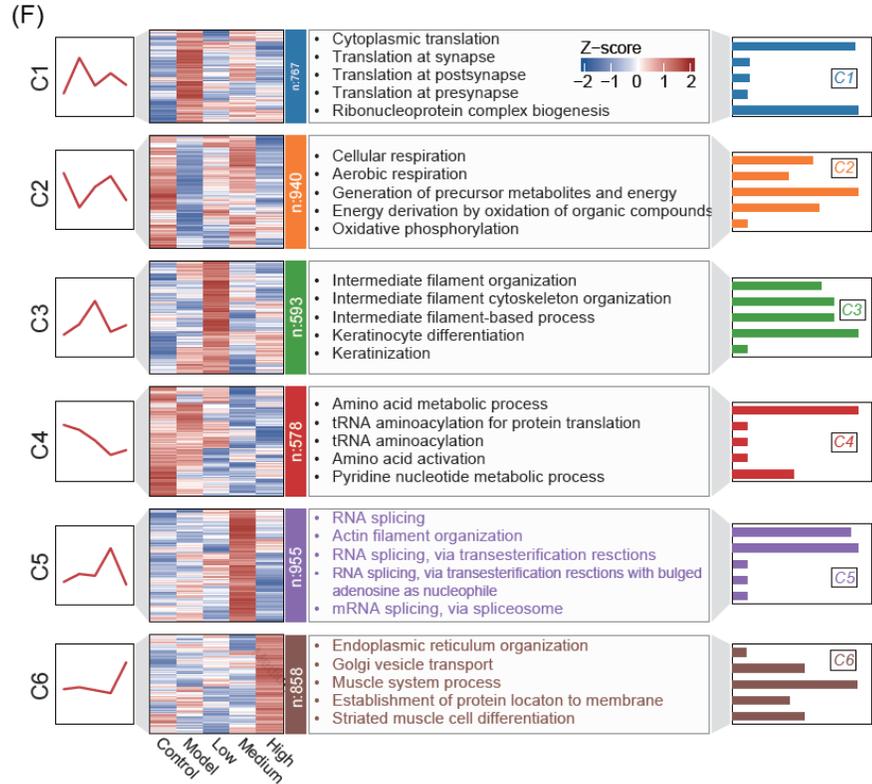


Figure 1. DCS enhances muscle regeneration and functional performance through remodeling of protein expression networks in myopathic mice.

Main result—chondroitin sulfate acts through the gut

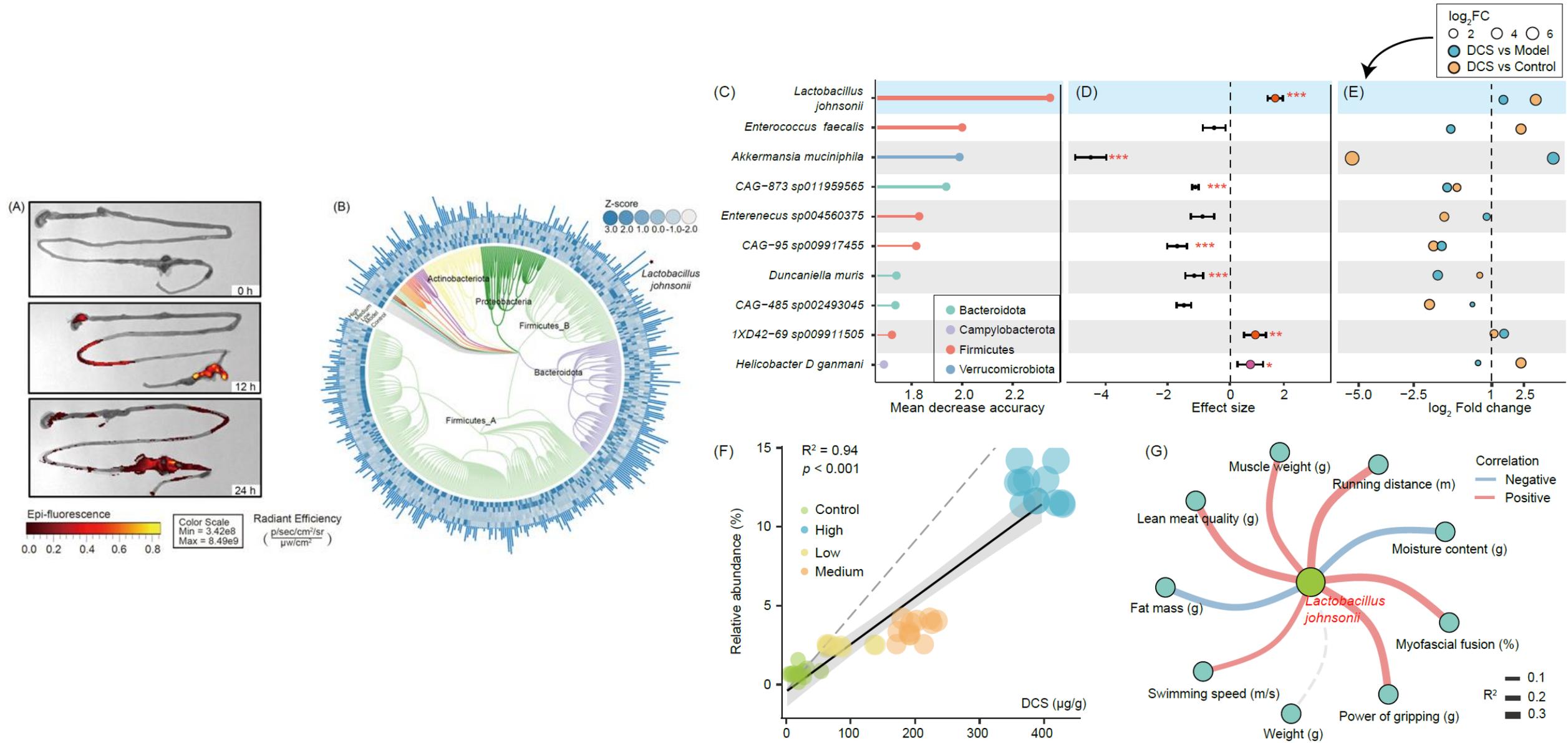


Figure 2. DCS reshapes gut microbiota and links microbial changes to muscle functional outcomes.

Speaker icon) Main result—Z-RW is gut target of chondroitin sulfate

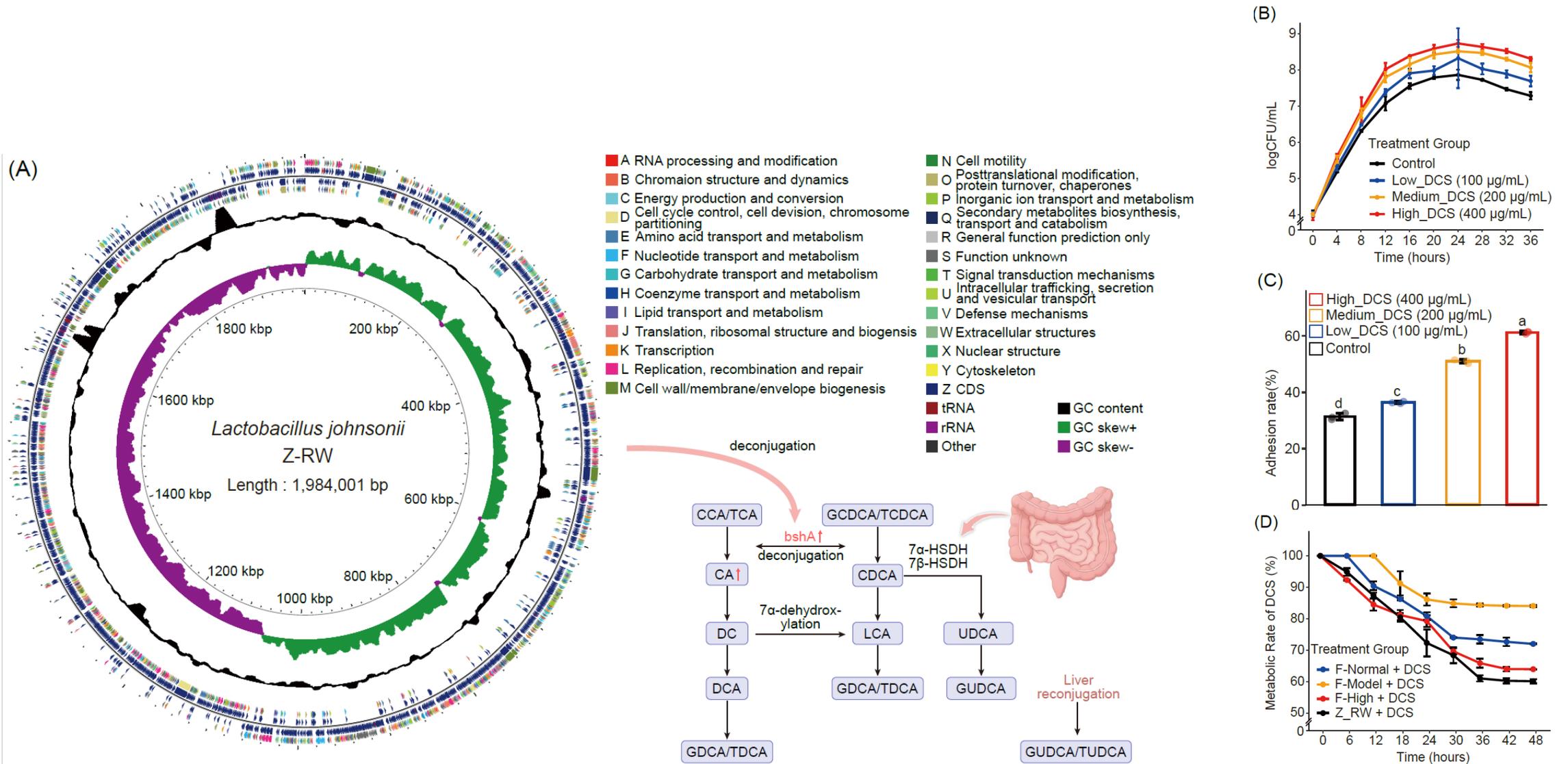


Figure 3. Dose-dependent effects of DCS on growth dynamics, adhesion behavior, and metabolic responses of *L. johnsonii* Z-RW.

Main result—chondroitin sulfate remodels gut metabolome

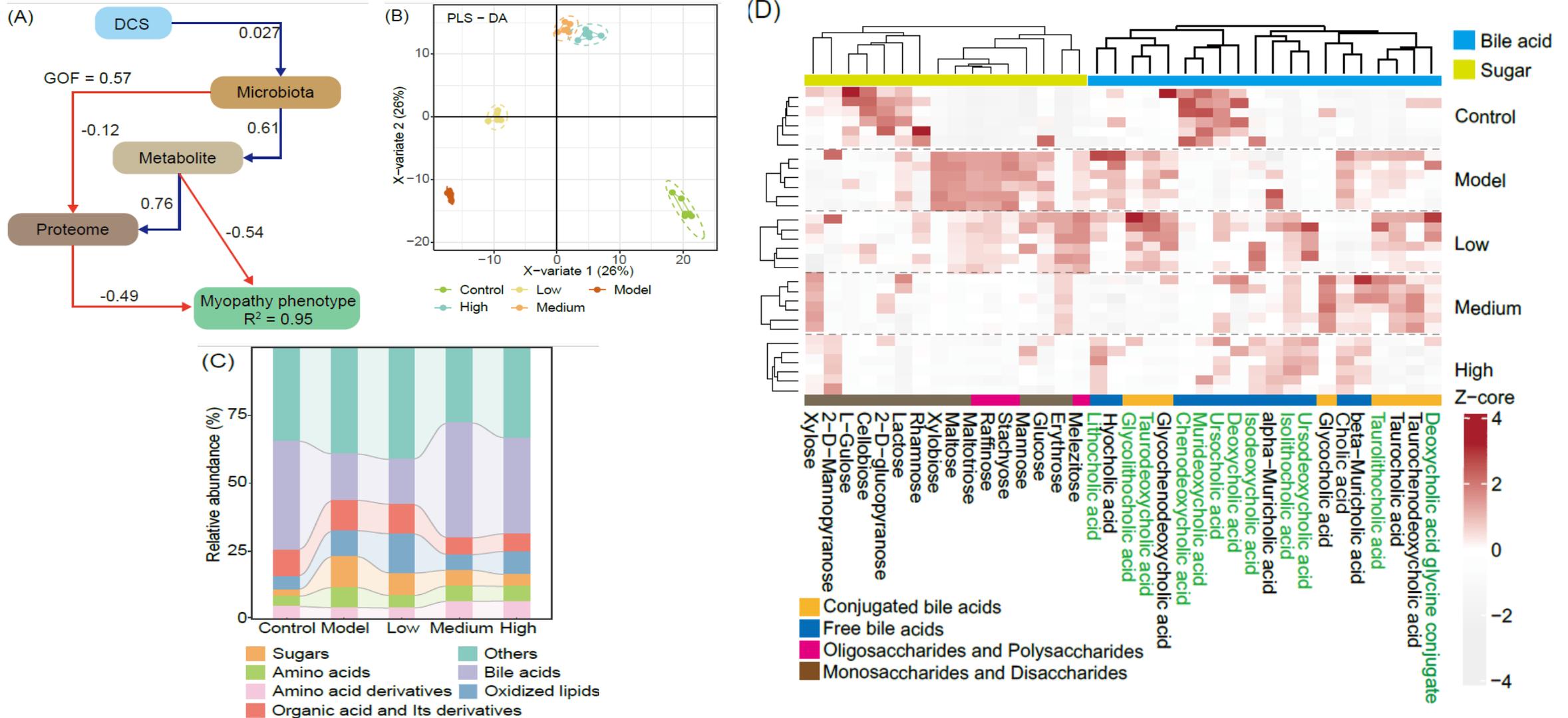


Figure 4. Integrated multi-omics analysis identifies key gut metabolites mediating muscle phenotypes and validates their functional effects in mice.

Main result—bile acids and Z-RW jointly drive muscle repair

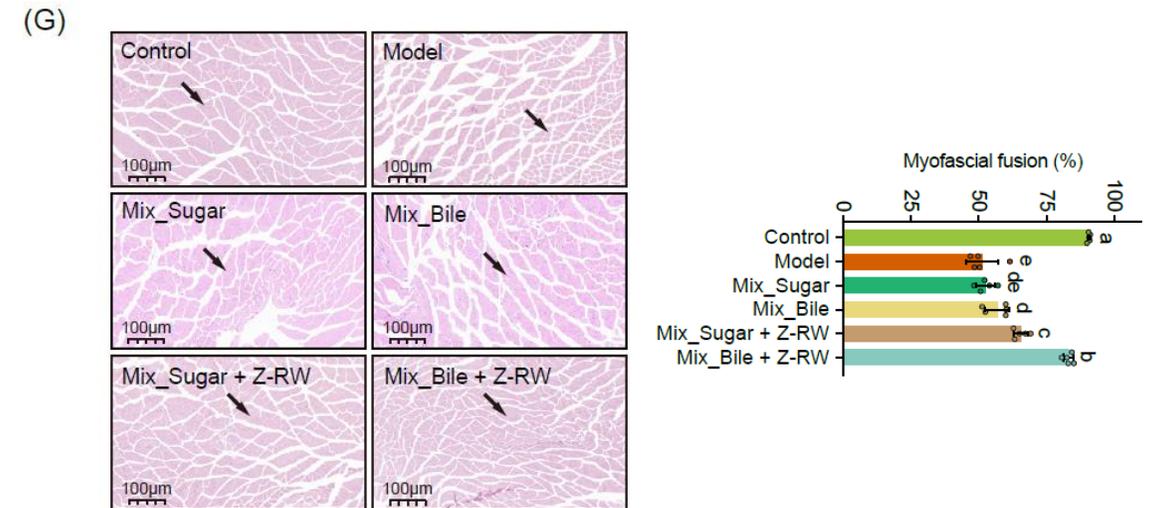
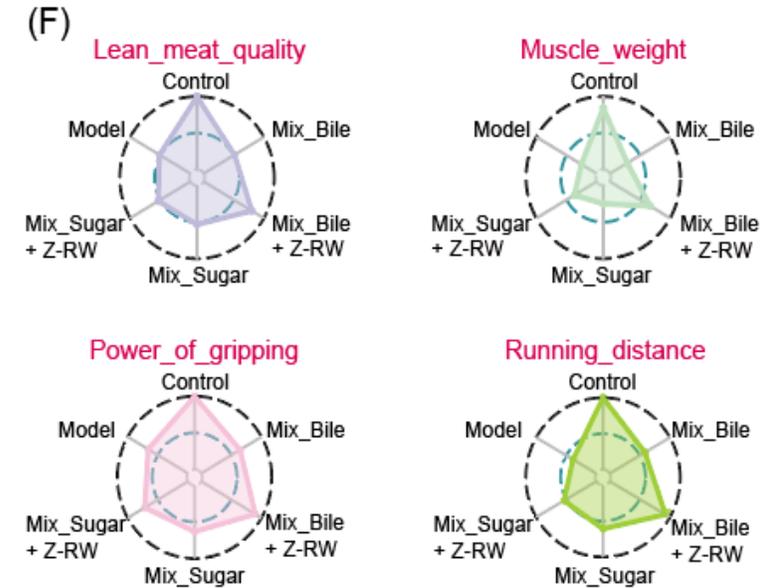
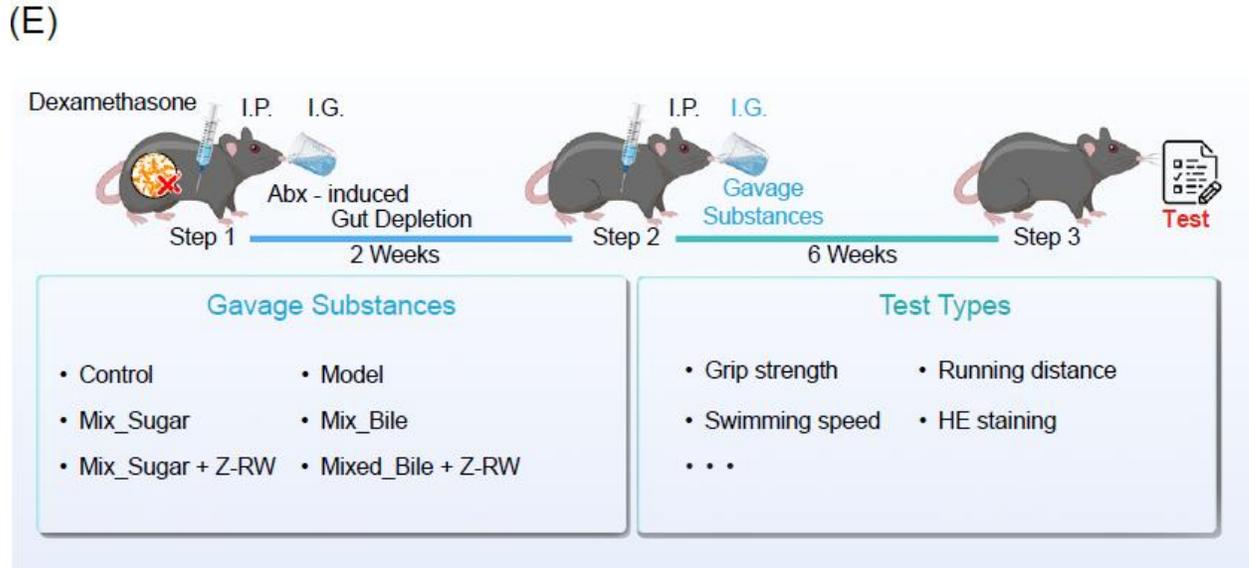


Figure 4. Integrated multi-omics analysis identifies key gut metabolites mediating muscle phenotypes and validates their functional effects in mice.

Main result—Z-RW regulates the gut sugar to bile acid ratio

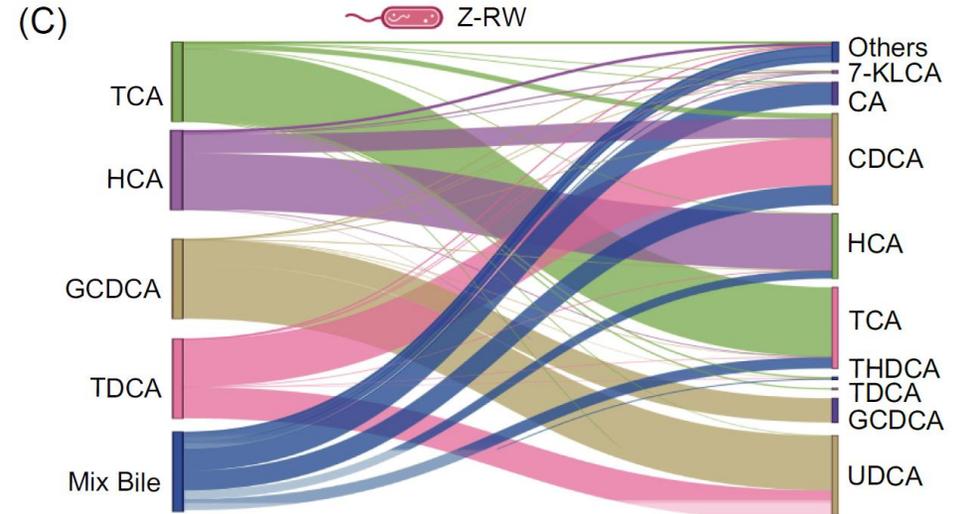
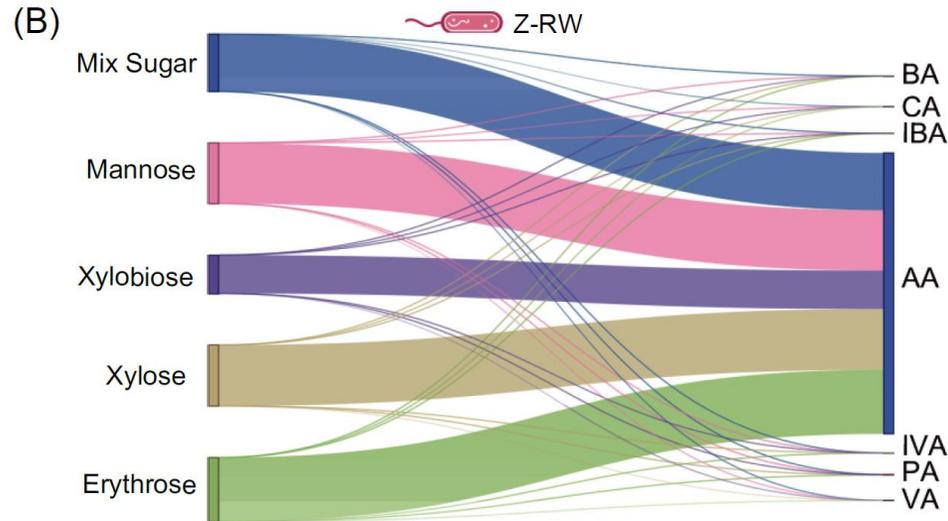
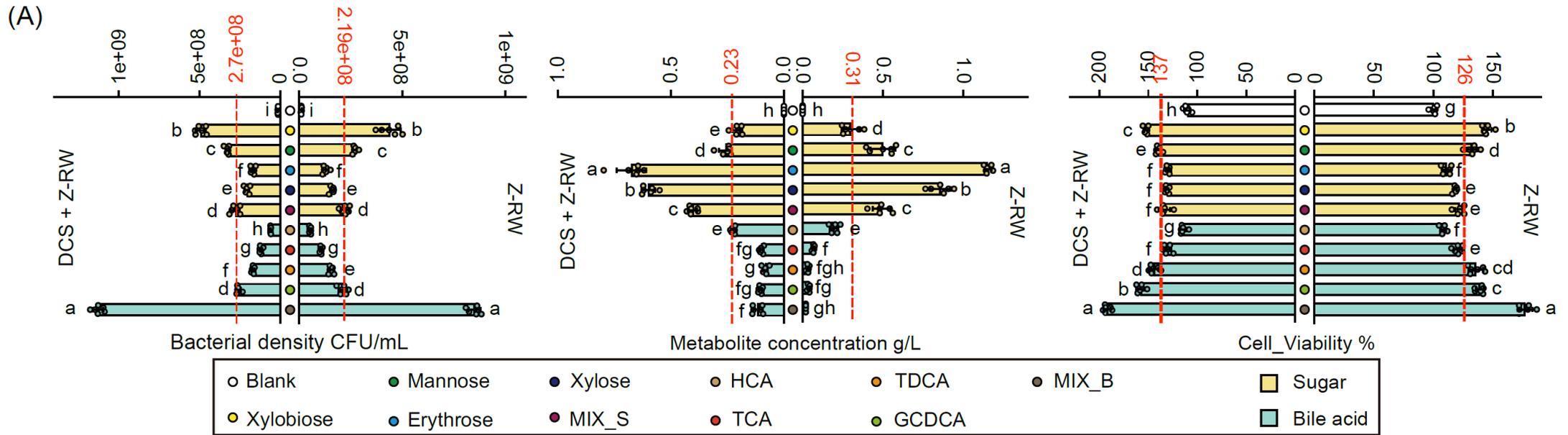
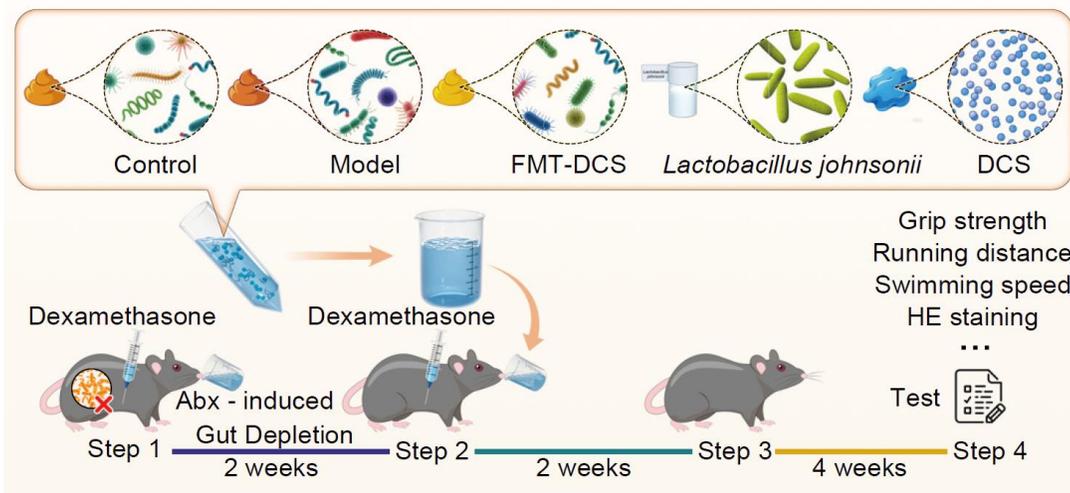


Figure 5. *L. johnsonii* Z-RW metabolizes gut sugars and bile acids and improves muscle function.

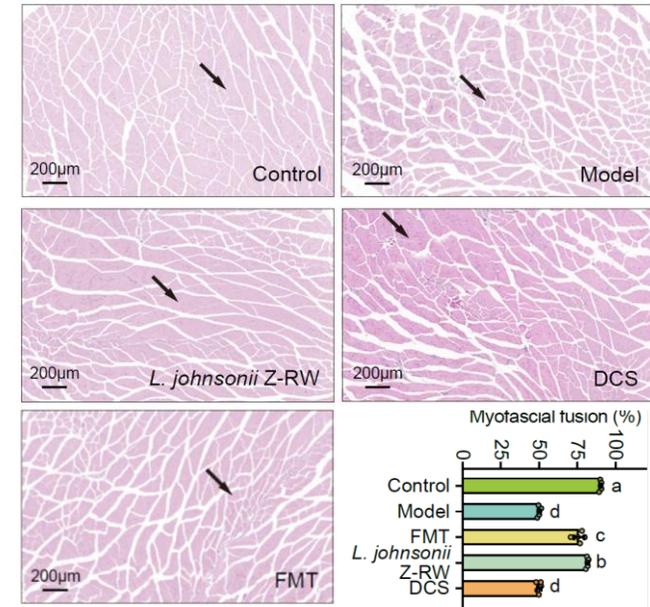
Main result—chondroitin sulfate restores sugar bile acid balance via Z-RW



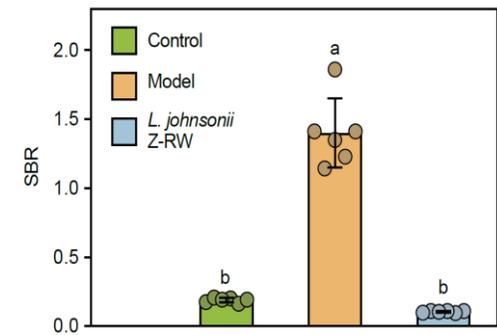
(D)



(F)



(G)



(E)

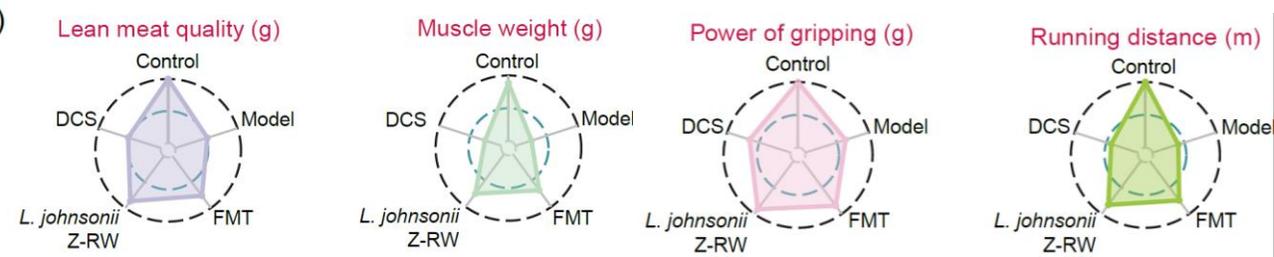


Figure 5. *L. johnsonii* Z-RW metabolizes gut sugars and bile acids and improves muscle function.

Main result—chondroitin sulfate restores sugar bile acid balance via Z-RW

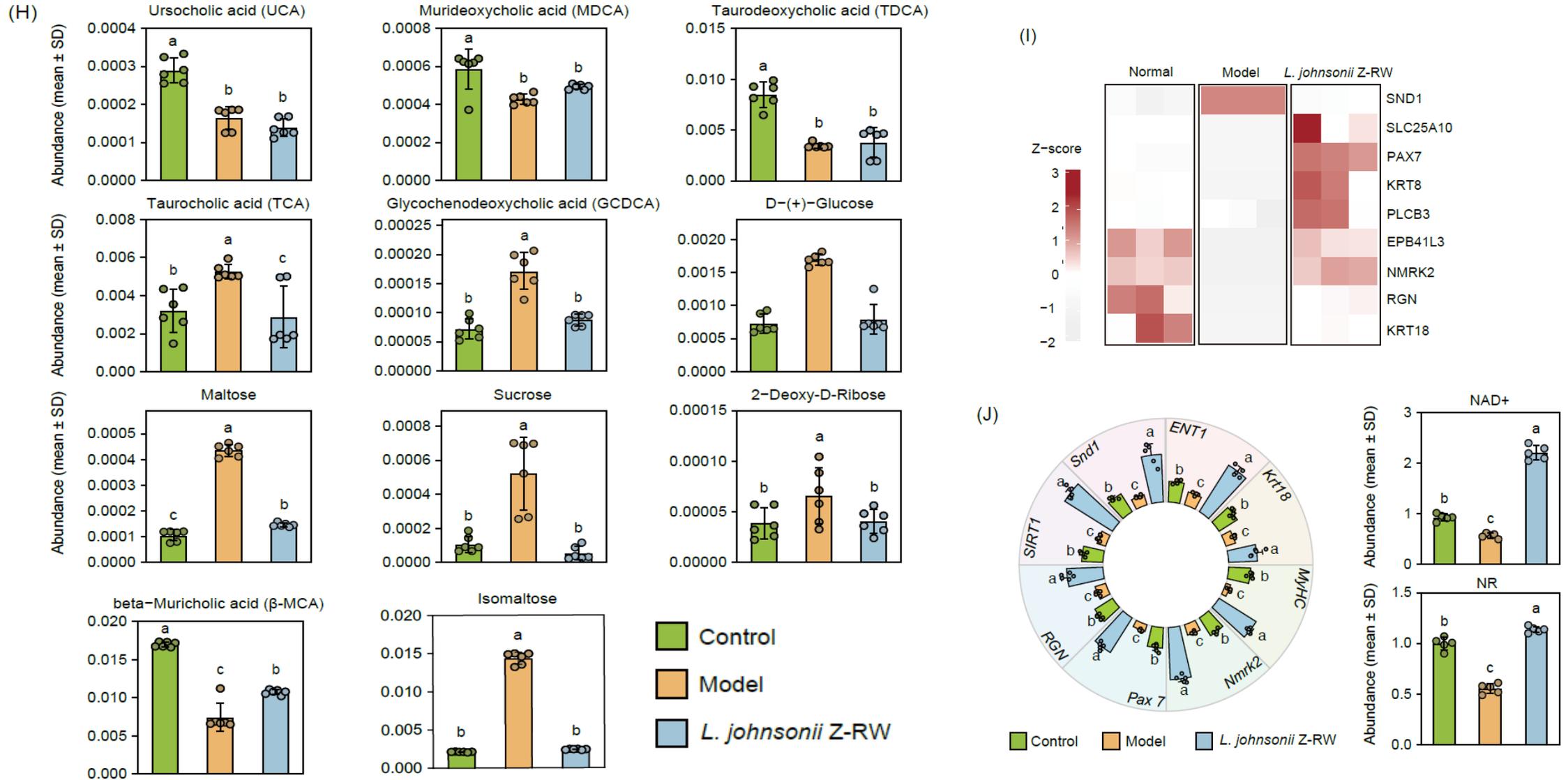


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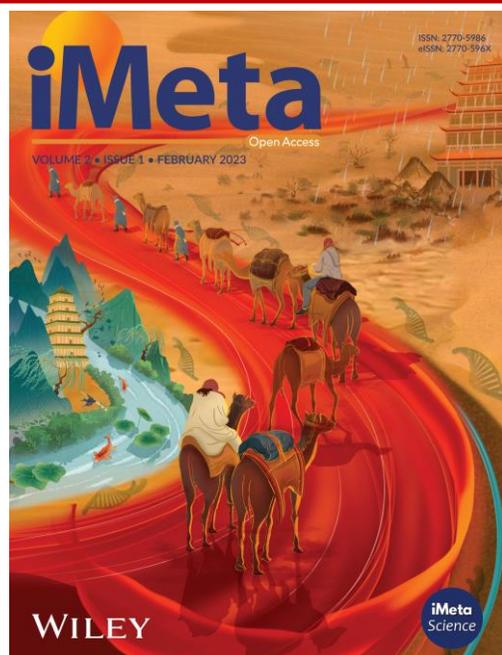
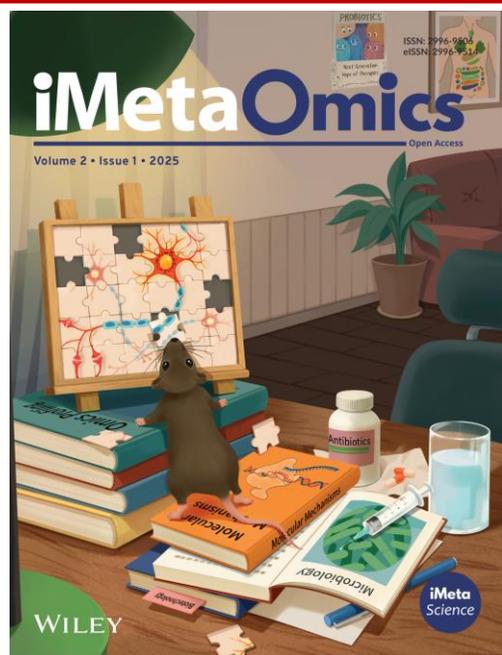
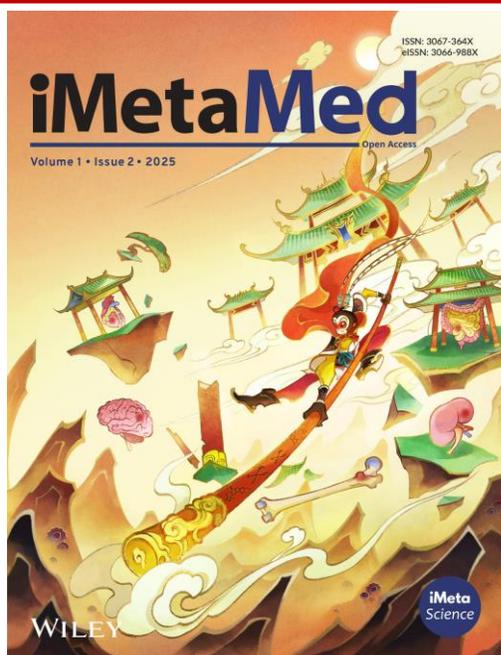


Summary

- ❑ In this study, we demonstrated that duck bone–derived chondroitin sulfate (DCS) can reverse muscle atrophy by remodeling the gut–muscle axis;
- ❑ Identified and isolated *Lactobacillus johnsonii* Z-RW as a key target strain mediating the in vivo effects of DCS; by recruiting and expanding Z-RW, DCS enhanced bile salt hydrolase–associated metabolism and thereby orchestrated the reprogramming of intestinal carbohydrate–bile acid metabolic networks;
- ❑ The metabolites generated through this intestinal metabolic reprogramming activated the PAX7/NMRK2 signaling pathway, thereby promoting muscle regeneration.

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