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Phenylalanine modulates innate immune of *Danio rerio* to clear ceftazidime resistant *V. alginolyticus*

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Antibiotic-resistant bacteria become a major threat to the economy and food safety in aquaculture. Although the antibiotic-dependent strategy is still the mostly adopted option, the development of antibiotic-free approach is urgently needed to ameliorate the severe situation of the global antibiotic resistance. In the present study, we showed that modulating the metabolism of zebrafish, *Danio rerio*, would enhance *D. rerio* to clear ceftazidime-resistant Vibrio *alginoyticus* (Caz-R) *in vivo*. By generating Caz-R *in vitro*, we found Caz-R stays longer than ceftazidime-sensitive *V. alginoyticus* (Caz-S) in D. rerio, where Caz-R induced less potent immune response than that of Caz-S. The differential immune response was associated with different metabolism of the host. Through functional metabolomics, we identified a crucial biomarker, phenylalanine. The abundance of phenylalanine was increased in both of Caz-S and Caz-R infected hosts but the abundance was higher in Caz-S infected group. This specific difference indicated phenylalanine could be a metabolite required to clear Caz-R by the host. Exogenous phenylalanine would enhance the host's ability to remove Caz-R, which was through upregulated production of lysozyme and C3b. Thus, our study demonstrates a novel strategy to boost host's immune response to combat against antibiotic-resistant bacteria.

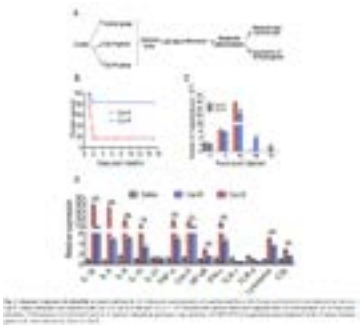

Figure: Immune response of zebrafish to Caz-S and Caz-R (A) Schematic representation of experimental flow (B) Percent survival of D. rerio infected by Caz-S or Caz-R. (C) Persistence of Cas-S and Caz-R in D. rerio by calculating gyrB gene copy numbers. (D) QRT-PCR for quantifying transcriptional levels of innate immune genes in D. rerio infected by Caz-S or Caz-R.

References:

1. Jiang, M., Gong, Q., Lai, S., Cheng, Z., Chen, Z., Zheng, J., & Peng, B. (2019). Phenylalanine enhances innate immune response to clear ceftazidime-resistant Vibrio alginolyticus in Danio rerio. Fish & Shellfish Immunology, 912-919.
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Biography

Ming Jiang is pursuing his Doctor's Degree at Sun Yat-sen University. His current research is focused on the metabolic mechanism of host resistance to drug-resistant bacterial infections.

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