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Malic acid boosted TCA cycle enhances survival of zebrafish to *Vibrio* alginolyticus infection

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Vibrio alginolyticus is a waterborne pathogen that infects a wide variety of hosts including fish and human, and the outbreak of this pathogen can cause a huge economic loss in aquaculture. Thus, enhancing host's capability to survive from *V. alginolyticus* infection is the key to fight infection and this remains still unexplored. In the present study, we established a V. alginolyticus-zebrafish interaction model by which we explored how zebrafish survived from *V. alginolyticus* infection. We used GC-MS based metabolomic approaches to characterize differential metabolomes between survival and dying zebrafish upon infection. Pattern recognition analysis identified the TCA cycle as the most impacted pathway. The metabolites in the TCA cycle were decreased in the dying host, whereas the metabolites were increased in the survival host. Furthermore, the enzymatic activities of the TCA cycle including pyruvate dehydrogenase (PDH), α-ketoglutaric dehydrogenase (KGDH) and succinate dehydrogenase (SDH) also supported this conclusion. Among the increased 3 metabolites in the TCA cycle, malic acid was the most crucial biomarker for fish survival. Indeed, exogenous malate promoted zebrafish survival in a dose-dependent manner. The corresponding activities of KGDH and SDH were also increased. These results indicate that the TCA cycle is a key pathway responsible for the survival or death in response to infection caused by *V. alginolyticus*, and highlight the way on development of metabolic modulation to control the infection.

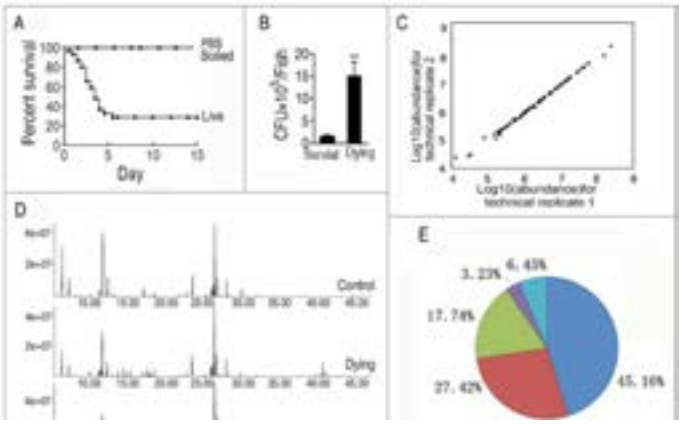

Figure: Metabolomic profiling of D. rerio humoral fluid. A: Percent survival of D. rerio infected with PBS (control 1, PBS), boiled V. alginolyticus (8 ×105 CFU/fish) (control 2, boiled), and sub lethal dose of V. alginolyticus (8 ×105 CFU/ fish) (live). B: Bacterial number of survival and dying fish after bacterial challenge. C: Reproducibility of metabolomic profiling platform. Metabolite abundances quantified in cell samples over two technical replicates are shown. Correlation coefficient between technical replicates varies between 0.990 and 0.999. This plot shows the two replicates with the weakest correlation of 0.990. D: Representative total ion current chromatogram from control (saline), dying and survival samples. E: Category of the identified metabolites.

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Biography

Manjun Yang is a lecturer of Tibet Vocational Technical College. He is pursuing his PhD from Sun Yat-sen University. His tutor is Prof. Xuanxian Peng who is a famous scientist of China. He has been committed to the research of bacterial antibiotic resistance. He is good at using metabolomic approaches based on GC-MS and UPLC/Q-TOF- MS platform to study drug resistance.

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