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Multi-omics analysis shed light on the mechanisms of tick reproductive inhibition by antibiotics*

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Ticks are vector pests and their biology and control are of worldwide concern. Microbiota play an important role in tick physiology, and antibiotic treatments are mostly used to explore the interactions between ticks and symbiotic microorganisms. In addition to altering the host microbial community, antibiotics also exhibit toxic effects on the host. In the tick *Haemaphysalis longicornis*, the engorged female ticks showed reproductive disruption after microinjection of tetracycline, as evidenced by prolonged oviposition time, reduced reproductive efficiency and hatchability, and abnormal oocyte development. Multi-omics approaches were implemented to unravel the mechanisms of tick reproductive inhibition in this study. The results showed that there were no significant changes in bacterial density in the whole ticks on days 2 and 4 after tetracycline treatment, while the bacterial microbial community significantly changed, especially on day 4. The relative abundance of the bacteria *Staphylococcus*, *Bacillus* and *Pseudomonas* decreased after tetracycline treatment, while the relative abundance of the bacteria *Coxiella* and *Rhodococcus* increased. Ovarian transcriptional response analysis revealed a cumulative effect of tetracycline treatment, as a significant increase in the number of differentially expressed genes with treatment time and a higher number of down-regulated genes. Several key tick physiological pathways such as lysosome, ECM-receptor interaction, ubiquinone and other terpenoid-quinone biosynthesis, insect hormone biosynthesis and focal adhesion were significantly inhibited after 4 days of tetracycline treatment. Metabolite levels differed after tetracycline treatment and the difference increased with treatment time. The differential metabolites were involved in a variety of physiological pathways, and the down-regulated metabolites were significantly enriched in the nicotinate and nicotinamide metabolism, galactose metabolism and Ether lipid metabolism pathways. These findings provide preliminary insights into the mechanisms by which tetracycline inhibits tick reproduction through regulation of tick bacterial communities, gene expression and metabolic levels, and may provide new strategies for tick control.

Keywords: Ticks, Tetracycline, reproductive anomalies, bacterial microbiota, transcriptome, metabolomics

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