Title: Tackling infectious disease and mental illness with *C. elegans*

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Alteration in gut microbiota influences not only host's survival but also memory and behavior. Due to the complexities of microbial interaction, host's immune and neuronal system, understanding of interactions between them has been limited. The free-living soil nematode *Caenorhabditis elegans* uses bacteria as a food source and has fixed number of neuronal cells. Mostly, *C. elegans* is isolated in decaying organic matters such as rotten fruit, where various microbe exists. Innate immunity of the nematode prevents infections by pathogenic microbes and its molecular components are well conserved with human's immune system. By conjugating the understandings of worm physiology to mechanism of human diseases, we developed a method of screening for discovering novel anti-infective compounds that can be a cure for infectious disease occurred by human opportunistic pathogens. We found three categories of anti-infectives, i.e. antibiotics, anti-virulent and immune-modulatory, from the screening. By using computer modeling-based chemical modification, we discovered new class of antibiotic compounds that rarely has drug resistance by microbes. In addition, we identified the mechanisms of immune-modulatory compounds by RNAi screening in *C. elegans.*

The nematode can also recognize differences between pathogenic and beneficial bacteria. The epithelial cells of *C. elegans* has a critical role in recognizing stress and inducing aversive learning behavior. However, the mechanism that relays the recognized stress from epithelial cells to neuronal cells have been less studied. We investigated epithelial cell derived molecules that can affect neuronal cells and modify aversive learning behavior. We found that knock-down of

neuropeptide processing enzymes alter aversive learning behavior. Based on these results, we tested all of 113 neuropeptides for their relevance to aversive learning behavior and found that two epithelial cell derived insulin-like neuropeptides regulate aversive learning behavior. More importantly, we found that control of aversive learning behavior is not limited to nematode's behavior but also influences energy storage and reproduction rate. Taken together, we could conclude that remembrance of noxious environment must be balanced, and feedback mechanism might allow this model host to actively balance in changing environments.