Chironomids and *Vibrio cholerae* – Friends or Foes?

Malka Halpern

[1]Dept of Evolutionary and Environmental Biology, University of Haifa, Mount Carmel, Haifa, 31905, Israel

Vibrio cholerae causes the fatal cholera diarrhea and is a natural inhabitant of aquatic ecosystems. Chironomids, (*Dipterae; Chironomidae*) are one of the most abundant insects in freshwater habitats. They undergo a complete metamorphosis of four life stages; eggs, larvae, pupae and adults. Chironomids were found to be a natural reservoir for *V. cholerae* and we commonly isolate *V. cholerae* along with other bacteria from all four life stages of chironomid insects. *V. cholerae* secretes Haemagglutinin/Protease (HAP) that degrades the gelatinous matrix of chironomid egg masses, likely acquiring nutrients and consequently preventing hatching. In a yearly survey *V. cholerae* and chironomids showed a pattern of a predator-prey population dynamics.

When chironomid microbiota that accommodate *V. cholerae* in the insect's habitat were studied, it was found that a large portion of the endogenous bacterial species in the insect was closely related to species known as toxicant degraders. Chironomids are known as pollution tolerant but little is known about their resistance mechanisms towards toxic substances. Bioassays based on Koch's postulates demonstrated that indeed, chironomid microbiome play a role in protecting their host from toxic hexavalent chromium and lead.

Quorum Sensing (QS) is a cell-cell communication process in which accumulation of secreted signal molecules (autoinducers, AIs) triggers an intracellular regulatory cascade. It has been shown that QS AIs induce HAP production in *V. cholerae* strains. To study the role of QS AI signals in HAP production by *V. cholerae* in mixed species consortia on chironomid egg masses, we used *V. cholerae* bioluminescence reporter strains (QS-proficient O1 El-Tor wild type and QS-deficient mutants). The findings demonstarted that *V. cholerae* responds to AIs produced by other members of the chironomid bacterial consortium by expressing the *hapA* gene. *V. cholerae*, a stable resident in chironomids is present in low prevalence. It degrades the egg masses by secreting HAP, prevents eggs from hatching and thus, exhibits host pathogen interactions with chironomids. However, the nutrients from the degraded egg masses may support the growth of the other microbiome members that have a role in protecting the host from toxicants and consequently control *V. cholerae* numbers. Therefore, the interaction between *V. cholerae* and chironomids is probably a complicated mutualistic relationship rather than a simple host–pathogen interaction.

Inter-species AI signaling to *V. cholerae* by bacteria in the intestine has recently been shown to alter the outcome of infection by reducing expression of the cholera toxin responsible for the profuse diarrhea. Understanding the interactions between *V. cholerae* and other endogenous bacteria in the insect host system may not only reveal complex relationships between this bacterium and its natural niche in aquatic settings, but may also provide insights into the interactions between this pathogen and commensal bacteria in the human gut. Perhaps, disease outcome in susceptible individuals could be altered with gut microbiota augmented to produce AI signals.