Comparing Double-Stranded RNA Uptake Mechanisms in Dipteran and Lepidopteran Cell Lines

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Abstract : While chemical insecticides effectively control many insect pests, they also harm many non-target species. Double-stranded RNA (dsRNA) pesticides, in contrast, can be designed to target unique gene sequences and thus act in a species-specific manner. DsRNA insecticides do not, however, work equally well for all insects, and for some species that are considered refractory to dsRNA, a primary factor affecting efficacy is the relative ease by which dsRNA can enter a target cell's cytoplasm. In this study, we are examining how different structured dsRNAs (linear, hairpin, and paperclip) can enter mosquito and lepidopteran cells, as they represent dsRNA-sensitive and refractory species, respectively. To determine how the dsRNAs enter the cells, we are using chemical inhibitors and RNA interference (RNAi)-mediated knockdown of key proteins associated with different endocytosis processes. Understanding how different dsRNAs enter cells will ultimately help in the design of molecules that overcome refractoriness to RNAi or develop resistance to dsRNA-based insecticides. To date, we have conducted chemical inhibitor experiments on both cell lines and have evidence that linear dsRNAs enter the cells using clathrin-mediated endocytosis, while the paperclip dsRNAs (pcRNAs) can enter both species' cells in a clathrin-independent manner to induce RNAi. An alternative uptake mechanism for the pcRNAs has been tentatively identified, and the outcomes of our RNAi-mediated knockdown experiments, which should provide corroborative evidence of our initial findings, will be discussed.

Keywords : dsRNA, RNAi, uptake, insecticides, dipteran, lepidopteran
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