

**EXECUTIVE SUMMARY [NON-CONFIDENTIAL, NON-TECHNICAL ABSTRACT FOR PUBLIC INFORMATION OR PROGRAM PROMOTION]:** State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project relevant to California. Do not include proprietary or confidential information. This may be distributed before the funding decision has been finalized.

The hornworm, *Manduca sexta*, is a strong model for studying regulation of behaviors leading to the removal of the old cuticle, or ecdysis. However, the ability to manipulate it genetically is limited, minimizing our ability to modify expression of peptides or genes of interest. Technologies such as RNA interference (RNAi) offer the potential to “knock down” or reduce specific gene expression in order to study their roles in physiological processes such as ecdysis. The peptide Ecdysis Hormone (EH) plays a major role in regulating ecdysis, but its actions have been difficult to characterize since it does not easily penetrate the nervous system (limiting our ability to assess its role after injection into the animal) and cannot be fully removed through genetic or surgical means. This proposal outlines experiments to develop RNAi technology with the aim of eliminating EH from identified cells. Developing the technology includes determining the best method of knocking down the gene (via ingestion or injection of RNAi components), and assessing the successful removal of EH from the nervous system through a variety of techniques. Ecdysis behaviors will be monitored in live animals and in isolated nervous systems. This technology will be applied under a number of experimental conditions, such as after injection of other critical ecdysis hormones, and to a variety of other neuropeptides whose sequences are known.