

6. Genetics of molting control

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We have begun genetic screens for new molting mutants in *C.elegans*. In insects, steroid hormones govern execution of the molting cycle by modulating the transcriptional activity of nuclear hormone receptors. Although the molting cycle in *C. elegans* also involves the activity of nuclear hormone receptors, the neuroendocrine control pathways upstream of these receptors remain unclear.

When exogenous cholesterol is excluded from the culture medium, wild-type worms arrest development in the second generation. The arrested larvae often fail to complete the molting cycle and become encased in old cuticle.

We used cholesterol deprivation to produce a sensitized genetic screen for molting mutants. Conditional mutants were isolated that arrest development at the L1 or L2 stage when cultured in the absence of exogenous cholesterol, but recover to form reproductive adults when transferred to a growth medium containing cholesterol. Five mutants were isolated that displayed an increased sensitivity to cholesterol deprivation in the first generation. Three of these mutants also displayed molting defects when cultured in the presence or absence of cholesterol. These mutants could be defective in the regulation and synthesis of or response to steroid hormones that normally regulate molting in *C. elegans*. Alternatively, these mutants could be primarily defective in cholesterol uptake or cholesterol homeostasis.