Functional analysis of CAP genes in *C. elegans*

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The Cysteine-rich secretory proteins, Antigen 5, and Pathogenesis-related 1 proteins, also known as CAP proteins, play significant roles in reproduction, development and sterol transport in various species, ranging from yeast to mammals. In *C. elegans*, 28 CAP homologues have been identified, most of which are referred as to SCL, with the exception of LON-1 and VAP-1. Some of the *scl* genes have been attributed a function but nevertheless, the molecular roles of CAP domain proteins in *C. elegans* remain to be uncovered. In yeast, the two CAP proteins Pry1 and Pry2 are necessary for sterol binding and export. Previously, our laboratory has complemented *pry1pry2* double mutants with *C. elegans scl* cDNAs, resulting in rescued sterol export in yeast. Considering these results, we hypothesized that CAP proteins are possibly involved in lipid metabolism and sterol transport in *C. elegans* as well. However, *C. elegans* CAP loss-of-function mutants did not show any obvious change in lipid droplet amount or distribution. On the other hand, vitellogenin, known to bind lipids and store sterols, was accumulating in the body cavity when multiple *scl* genes were lacking. Such mutants are reminiscent of old wild type worms in terms of yolk accumulation. Furthermore, when grown in low-cholesterol conditions, *scl* mutants developed slightly faster, had less oogenesis defects, and had no significant decrease in their brood size. By combining multiple *scl* mutant alleles, no other mutant phenotype was observed except the long phenotype in *lon-1* mutants indicating that worm *scl* genes might be at least partially redundant with each other. Nonetheless, when combining a *scl-17* mutant allele with the *chup-1(gk245)* mutant known to be defective in cholesterol uptake, we observed the emergence of age-related pathologies. Finally, in order to analyse the function and expression pattern of *scl* genes, different reporter transgenes were generated. Interestingly, most of the transgenes are expressed in head or tail neurons. Additionally, SCL-17 and SCL-10 proteins are attributed a secretory capacity, since they were detected in the vesicles of the coelomocytes. Our results also suggest that *scl-9* and *lon-1* expression is modulated by cholesterol and dependent on *scl-1*. Overall, we provide several lines of evidence that at least some of the worm *scl* genes are involved in stress resistance, cholesterol metabolism and fertility.

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