Using Collagen-19 Expression in Caenorhabditis elegans Development to Further Expand the let-7 microRNA Genetic Interactome

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MicroRNAs (miRNAs), small noncoding RNA genes, play crucial roles in regulating gene expression in human development and cancer. The let-7 miRNA is involved in various cellular processes, including cell division, differentiation, and programmed cell death. let-7 acts as a tumor suppressor gene, preventing cancer cells from forming, though its precise mechanisms are not fully known. This study aims to clarify the genetic basis of let-7 function by studying adult cuticle formation and hypodermal maturation in the roundworm nematode, Caenorhabditis elegans. Larval development in worms follows a precise genetic clock requiring let-7 to synchronize terminal differentiation across tissues, such as driving expression of the adult-specific collagen col-19 in hypodermal cells after the juvenile to adult transition. To identify potential downstream targets for let-7 regulation, RNA interference (RNAi) was performed in a strain made by genetic crosses with a let-7 mutation and a pCol-19::gfp reporter, a transgene for col-19 transcriptional activation of a green fluorescent protein, to knock down candidate genetic interaction partners. Observing that pCol-19::gfp expression was lost in let-7 mutants, RNAi depletion of downstream targets was expected to restore pCol-19::gfp expression. After performing RNAi targeting known let-7 targets lin-41 and daf-12, pCol-19::gfp expression was observed, confirming the sensitivity of the pCol-19::gfp reporter in identifying potential let-7 targets. Identifying these target genes will enhance the understanding of let-7 genetic interactions and its broader roles in developmental timing, cell proliferation and differentiation. Ultimately, this study aims to provide insights into the let-7 tumor suppressor regulatory pathways in human cancer.

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