The Conserved NAB family Transcriptional Co-factor *mab-10* Acts with the Heterochronic Gene *lin-29* to Regulate Terminal Differentiation in Hypodermal Lineages

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The study of heterochronic mutants has revealed a complex genetic pathway that regulates the timing of many developmental events in *C. elegans.* Heterochronic mutants fall into two classes: precocious mutants, which prematurely express later developmental fates, and retarded mutants, which reiterate earlier developmental fates. Both classes can alter the timing of the larval-to-adult transition. This transition comprises four events: seam cell fusion, generation of an adult-specific cuticle, exit of seam cells from the cell cycle, and exit from the molting cycle.

Like retarded *let-7* and *lin-29* mutants, *mab-10* males undergo an extra molt approximately 18 hours after the larval-to-adult transition (C. Link, Worm Breeder's Gazette 10, 92, 1988). To understand further the regulation of the larval-to-adult transition, we have analyzed *mab-10* and found that both *mab-10* males and hermaphrodites enter lethargus as adults and often execute an extra molt. While the seam cells of *mab-10* mutants fuse appropriately at the end of the L4 stage and generate a relatively normal adult cuticle, the seam cell nuclei of *mab-10* mutants inappropriately undergo extra rounds of division. We conclude that *mab-10* is required for the prevention of seam cell divisions and for the cessation of molting, but is not required for seam cell fusion or adult cuticle synthesis. By contrast, the C2H2 zinc finger protein LIN-29 is required for all four events during the larval-to-adult transition.

We cloned *mab-10* and found that it encodes the only *C. elegans* member of the conserved NAB (NGFi-Alpha Binding) family of transcription factors. Recent studies of mice have implicated the NAB family of proteins in regulating the terminal differentiation of specific stem cell lineages (Le et al., Nature Neurosci. 8, 932, 2005). NAB proteins are believed to act as co-factors for C2H2 zinc fingers to regulate differentiation. Our genetic analyses and co-localization and *in vitro* binding experiments suggest that MAB-10 functions as a cofactor for the C2H2 zinc finger transcription factor LIN-29 to regulate specifically the exit of the seam cells from the cell cycle and the cessation of molting, but not seam cell fusion or adult cuticle synthesis. We propose that the regulation of developmental stage in *C. elegans* and the regulation of terminal differentiation in mammalian stem cell lineages share a common mechanism controlled by a conserved heterochronic pathway.

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