

## The evolutionarily conserved DEAD-box helicase DDX-23 functions in stem cell biology

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During animal development, gene regulation needs to be temporally precise for proper cell-fate decisions to occur. The evolutionarily conserved *C. elegans* heterochronic pathway controls the temporal progression of development by regulating the activities of a sequence of genes. Components of this pathway control cell-fate decisions of proliferation versus differentiation, and mammalian homologs of these components play critical roles in stem cell regulation and cancer biology.

*mab-10* encodes the *C. elegans* NGFI-A-binding protein (NAB) transcriptional co-factor. MAB-10 is involved in the terminal differentiation of the hypodermal stem-like seam cells and more generally in the larval-to-adult transition. LIN-29, the master regulator of the larval-to-adult transition, is an early growth response (EGR) protein that acts together with MAB-10 to control the expression of genes that regulate the onset of adulthood and terminal differentiation in the hypoderm. Strikingly, EGR proteins interact with NAB proteins to cause terminal differentiation and the onset of puberty in mammals. Despite the importance of this pathway, mechanisms by which the terminal effectors LIN-29(EGR) and MAB-10(NAB) function remain largely unknown.

We are studying LIN-29(EGR) and MAB-10(NAB) with the goal of understanding the mechanisms that control *C. elegans* developmental timing and providing insights concerning stem cell identity and development in mammals. We performed genetic screens for enhancers of the *mab-10* mutant phenotype and identified the DEAD-box helicase gene *ddx-23* as a regulator of seam cell fate. We showed that DDX-23 functions in the seam cells to regulate seam cell exit from the cell cycle. Our data suggest that DDX-23 and MAB-10 act in a complex to regulate the decision for the seam cells to terminally differentiate. We propose that this interaction is evolutionarily conserved and act to regulate mammalian stem cell development. We hope to elucidate the exact mechanism by which DDX-23 and MAB-10 function in stem cell biology.

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