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The role of RNA-binding proteins in orchestrating germline development in *Caenorhabditis elegans*

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RNA passed from parents to progeny controls several aspects of early development. The germline of the free-living nematode *Caenorhabditis elegans* contains many families of evolutionarily conserved RNA-binding proteins (RBPs) that target the untranslated regions of mRNA transcripts to regulate their translation and stability. In this review, we summarize what is known about the binding specificity of *C. elegans* germline RNA-binding proteins and the mechanisms of mRNA regulation that contribute to their function. We examine the emerging role of miRNAs in translational regulation of germline and embryo development. We also provide an overview of current technology that can be used to address the gaps in our understanding of RBP regulation of mRNAs. Finally, we present a hypothetical model wherein multiple 3'UTR-mediated regulatory processes contribute to pattern formation in the germline to ensure the proper and timely localization of germline proteins and thus a functional reproductive system.

KEYWORDS

RNA-binding proteins, nematode, germline, post-transcriptional regulation, embryogenesis, oogenesis, translation

Introduction

In sexually reproducing organisms, post-transcriptional regulation of maternal and paternal mRNAs is crucial to gametogenesis and early embryo development (Wickens, 1999; Richter, 1991; Curtis et al., 1995; DeRusso and Seydoux, 2004; Farley and Ryder, 2006; Kang and Han, 2011). During embryogenesis, control of the levels and localization of specific mRNAs and proteins is key for axis formation and cell fate specification (Zhang et al., 2014). Components of these regulatory processes include RNA-binding proteins (RBPs) and/or regulatory small RNAs that affect the stability of the mRNA transcript and ultimately influence protein levels (Shaw et al., 2010). Delineating the mechanisms of post-transcriptional regulation and how they mediate transfer of information from parent to progeny at the mRNA level will provide a deeper understanding of reproduction and early development as well as how misregulation of such processes can lead to disease.

C. elegans is a well-suited model organism to study the biology of RBP-mRNA networks and how they regulate early development. They have a large brood size (~300), develop from an egg to an adult in a short time (2–3 days), and are self-fertile (Cori et al., 2015). Not only is this nematode easy to grow and maintain, but there is a plethora of genetic and biochemical techniques that enable addressing important questions in the field of RNA regulation in this organism. CRISPR/Cas9 genome editing is straightforward in the worm and has become a standard technique for genetic manipulation (Kim and Colasacco, 2019; Vicente and Ceron, 2021). Many of *C. elegans* developmental and molecular phenotypes are easy to score and analyze (Cori et al., 2015). Additionally, both *in vivo* and *in vitro* biochemical methods have

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novel regulators in normal development of sexual dimorphisms including the differentiation of ovaries and testes the genital tract including prostate epididymis and uterus as well as mammary glands In addition particular attention is paid on their role in pathophysiological processes within the reproductive tract The power of next generation sequencing has proved to be an invaluable tool to discover new non coding RNAs While the identification of non coding RNA is relatively easy analysing their function represents still a challenge today In this book authors present historical and conceptual background information highlight the ways in which non coding RNAs function is analysed and present their vision of the future research in their key research area

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