Identification and Characterization of the Two *C. elegans* Asf1 Histone Chaperone Homologs

by

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ABSTRACT

Within the nucleus, the eukaryotic genome is highly organized into fundamental chromatin units by means of chromatin-associated proteins. One of these important chromatin-associated proteins is Anti-silencing function 1 (Asf1), a highly conserved histone chaperone involved in a variety of cellular mechanisms. In some higher eukaryotes, Asf1 is found in two isoforms. However, the developmental roles of Asf1 and the mechanisms by which Asf1 mediates diverse molecular pathways are poorly understood. The nematode worm, *Caenorhabditis elegans* has two Asf1 homologs encoded in its genome. In this study, the molecular identity of the *C. elegans unc-85* gene is revealed to encode one of the two homologs of Asf1. The gene expression of *unc-85* is stringently regulated during development, and the protein is found in the nuclei of actively replicating somatic cells and in the germline. Measurement of the DNA content of *unc-85* mutant neurons in the ventral cord reveals defective replication with the average DNA content of approximately 2.5n, suggesting that UNC-85 functions in S-phase of post-embryonic cell divisions of the ventral cord neuroblasts. The second gene encoding *C. elegans* Asf1 histone chaperone homolog, *asf1-like* (*asfl-1*), is expressed in the meiotic region of the germline and in early embryos. Mutants in either Asf1-encoding gene exhibit reduced brood sizes (80% of the wild-type) and defective gametogenesis with low penetrance. However, the double mutants are sterile, displaying severe defects in gametogenesis, and increased germline apoptosis. Somatic tissue phenotypes observed in *unc-85* mutants are neither observed in *asfl-1* mutants, nor enhanced in the double mutants. Furthermore, only UNC-85 is required for two conserved acetylations of histone H3 on K9 and K56 during development. In summary, UNC-85 appears to be solely responsible for ensuring proper somatic functions and the acetylation of histone H3 on K9 and K56, while ASFL-1 and UNC-85 have overlapping functions in the germline to promote proliferation and gametogenesis.