Abstract

Members of the MYST family of histone acetyltransferases (HATs) are found in eukaryotes from yeast to human. They covalently attach acetyl groups to lysine residues of the core histones as well as of other proteins. With this function, they affect the structure of chromatin and influence elementary cellular processes like transcription, DNA replication and DNA repair. Global acetylation of lysine 16 on histone H4 (H4K16Ac) has been found to be dependent on the conserved homologues Sas2 (*Saccharomyces cerevisiae*), dMOF (*Drosophila melanogaster*) and hMOF (*Homo sapiens*) in their respective species, and they are components of multi-protein complexes. Their acetylation activity is regulated by additional complex subunits. Dosage compensation in flies is mediated by dMOF, and as part of the MSL complex, it acetylates H4K16 on male X chromosomes, leading to increased X-linked transcription.

MYS-2 is a histone acetyltransferase of the MYST family from the model organism *Caenorhabditis elegans*. Little is known about MYS-2 function, though it has been reported to influence cell identity and to mediate inheritance of RNA interference. Here, we report that MYS-2 is ubiquitously expressed in worms, and that it has an essential function in the worm and influences early embryogenesis. MYS-2 was found to be expressed throughout development in germ cells and somatic tissues, including the first stages of embryogenesis. The main portion of MYS-2 was found in nuclei, where it colocalized with DNA. Furthermore, the absence of MYS-2 was lethal. MYS-2-depleted animals were rescued to wild-type phenotype by a maternal contribution of *mys-2* gene products, and incomplete rescue with residual levels of *mys-2* gene products caused severe developmental defects. Growth rate, general morphology and particularly the vulva, the somatic gonad and germ cell nuclei were affected. These findings are consistent with reported effects of other chromatin modifiers in *C. elegans*, for instances the HAT CBP-1 or the histone deacetylases HDA-1. In contrast to reports on the close homologues Sas2, dMOF and hMOF, a significant impact on global levels of H4K16Ac was not observed. In an interactor screen, a number of candidates were found that include a potential subunit of a MYS-2 containing HAT complex and histone H3 as a potential acetylation substrate. In summary, our data suggest a function for MYS-2 in early embryogenesis, presumably in the regulation of global transcription in a chromatin-dependent manner.