A Comprehensive Expression Map of Lysine Methyltransferases Reveals Germline-specific Function of *set-17*

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Posttranslational modification of histone tails is fundamental to controlling access to DNA. Lysine methyltransferases (KMTs) methylate lysine residues in histone tails to specify transcription or silencing. In humans, KMTs have been implicated in important biology, such as fertility, and disease, such as cancer. The SET domain is catalytically active in KMTs. The C. elegans genome encodes 38 putative KMTs, most of which have plausible mammalian orthologs. In C. elegans, four KMTs are required for viability and four KMTs have been implicated in germ cell fate specification; individual mutation or RNAi inactivation of the remaining KMTs revealed no other gross defects.[1]

To analyze KMT function, we determined the endogenous mRNA expression profile of all KMTs in early L1 larvae using single molecule fluorescence in situ hybridization (smFISH). For each KMT, we created a smFISH probe-set of 48 DNA oligos. These probe-sets now constitute a comprehensive freely available resource to study endogenous KMT expression. In L1 larvae, most KMTs are expressed in a tissue-specific manner. Only ten KMTs are expressed broadly throughout the animal. Four KMTs display a muscle-specific expression pattern and four KMTs are expressed exclusively in the germline. Overall, 22 KMTs are expressed in the two primordial germ cells, Z2 and Z3.

To investigate KMT function in the germline, we determined the brood size of all available mutants of germline-expressed KMTs. Four single KMT mutants show brood size defects: *met-1*, *met-2, set-17* and *set-32. set-17* is an uncharacterized broadly expressed KMT with a PR-type SET domain, the closest mammalian orthologs of which are PRDM9 and PRDM7. Loss of *set-17* causes a reduction in sperm number. A rescuing *set-17*::GFP single-copy transgene shows that SET-17 localizes in sparse foci (~5-8) to diplotene nuclei in both sperm and oocyte precursors. Based on these data, we propose that *set-17* functions in germ cell maturation or meiosis.

The expression data and smFISH resource provide the basis for further specific investigation of the function of KMTs in C. elegans biology.

1 Andersen and Horvitz, Development, 134, 2991-9, 2007