Use of Single-molecule FISH To Determine Expression Patterns and Functions of *C. elegans* Lysine Methyltransferases

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The family of lysine methyltransferases (KMTs) can regulate access to the genome by methylating lysine residues in the N-terminal tails of histones. In humans, several KMTs have been implicated in disease, such as cancer. In the *C. elegans* genome, 41 putative KMTs have been identified. Four KMTs are essential for viability. Five have been shown to act to generate or maintain the germline, or to inhibit ectopic vulval development. A systematic analysis of the remaining KMTs revealed few gross defects after mutation or RNAi inactivation of individual KMT genes. Three-quarters of the *C. elegans* KMTs have plausible mammalian orthologs.

To investigate KMT function in *C. elegans*, we have determined the cell-specific expression patterns of the 41 KMT genes in the L1 and L3 larval stages using single-molecule fluorescence *in situ* hybridization (smFISH). smFISH enables the determination of expression of single molecules of endogenous mRNAs throughout the entire animal.² Our analysis showed that ten KMTs are expressed throughout the animal. Fifteen KMTs are expressed in a single tissue, such as *set-6* in muscle and *set-20* in the hypoderm. Six and four KMTs are expressed exclusively in the germline or the muscle, respectively. In addition, several KMTs are expressed in the seam cells but not in other hypodermal cells. Based on these observations, we are designing experiments to identify the functions of KMTs in these tissues. We will also use these KMT expression patterns to investigate whether functional redundancy among certain KMTs can account for the apparently wild-type phenotypes of animals lacking the functions of many individual KMT genes.

We hope our analysis will define KMT functions and interactions in specific *C. elegans* tissues and suggest possible roles of worm KMT homologs in mammalian biology.

1 Andersen and Horvitz, Development, <u>134</u>, 2991-9, 2007

2 Raj *et al.*, Nat Methods, <u>5</u>, 877-9, 2008

Poster

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