Elucidating the Role of Putative Histone Lysine Methyltransferases in *C. elegans* by Combining Expression and Genetic Analyses

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Post-translational methylation of the histone tails is an important and conserved modification that regulates transcription. Lysine methyltransferases (KMTs) mediate this methylation. In the *C. elegans* genome, 39 putative KMTs have been identified. While three KMTs are essential, only five of the remaining 36 have been implicated in biological processes: a systematic genetic analysis of KMTs inactivated by mutation or reduced in activity by RNAi revealed few defects[1]. It is possible that this result is due to redundancy among multiple KMTs or between KMTs and other transcriptional regulators. Alternatively, abnormal phenotypes of single KMT mutants could be subtle or delayed by multiple generations. To further analyze KMT function, we will conduct a comprehensive study of the expression patterns of the 39 KMT genes in *C. elegans*. To this end, we are using single-molecule Fluorescence *In Situ* Hybridization (smFISH), a technique that enables the quantification of endogenous mRNA expression in the entire animal with single molecule resolution[2]. Expression patterns restricted to specific cells or tissues might suggest that single mutants harbor very specific phenotypic abnormalities, which we will attempt to identify. For KMTs that are co-expressed, we can predict and test synthetic interactions that might elicit phenotypic abnormalities. Our preliminary data show tissue-specific expression and overlap for many of the putative KMT genes. For ubiquitously expressed KMTs, we have observed different levels of expression among cells and tissues, suggesting specific roles in these contexts. Some cells and tissues express large numbers of KMTs. We hope that our approach will allow us to comprehensively analyze the role of KMTs in metazoan biology.

[1] Andersen and Horvitz, Development, 134, 2991-9, 2007
[2] Raj, van den Bogaard, Rifkin, van Oudenaarden and Tyagi, Nat Methods, 5, 877-9, 2008

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