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## "TET enzymes regulate gene expression by a non-canonical mode of action in the fly"

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The development of diseases is often associated with changes in the activity of epigenetic enzymes, which are crucial regulators of gene expression and thus cell function. For example, mutations affecting enzymes of the TET (Ten Eleven Translocation) family are associated with different pathologies, notably in the hematopoietic and nervous systems. While the role of TET in the oxidation and demethylation of 5-methylcytosine (5mC) in DNA is well established in vertebrates, these enzymes also have other substrates and catalytic-independent functions that remain poorly understood. Interestingly, the Drosophila genome is essentially devoid of 5mC but still encodes for well-conserved TET enzymes, making this insect an ideal model to better characterize TET functions beyond 5mC oxidation. Accordingly, we take advantage of this model organism to decipher the non-canonical functions of TET and its molecular mode of action in the larval central nervous system (CNS). By using a combination of genetic and molecular approaches, we show that TET controls the expression of many genes in the larval CNS and that its mutation leads to neuron patterning defects. In this tissue, TET binds regulatory elements along the genome and in many instances colocalizes with Polycomb-group proteins, major players in gene expression regulation. Further experiments suggest that PRC1 (Polycomb Repressive complex 1) is also involved in the regulation of TET target genes. Moreover, the analysis of a point mutant in which TET enzymatic activity is abolished reveals that an important part of TET functions is independent of its catalytic activity. Altogether, our results bring a better understanding of the diversity of TET modes of action in the regulation of genome expression.