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REVISITING THE ROLE OF THE TET EPIGENETIC ENZYME IN DNA DEMETHYLATION AND GENE EXPRESSION REGULATION IN DROSOPHILA

7.NOVEMBER 2023 - 11 AM - LECTURE HALL

Members of the Ten Eleven Translocation (TET) family are well known for their role in the oxidation and demethylation of 5-methylcytosine (5mC), a prevalent epigenetic mark in vertebrates. Yet, these epigenetic enzymes also seem to have other substrates and enzymatic-independent functions, which are less well characterized. The Drosophila genome is largely devoid of 5mC and does not code for DNMT but presents a single and well-conserved *Tet* gene. This organism thus represents a well-suited model to decipher the non-canonical (5mC DNA-independent) functions of TET enzymes. Recently the presence of 6-methyladenine (6mA) in DNA has been reported in various eukaryotes. In drosophila, this epigenetic modification was shown to be erased by TET. Yet, the existence and significance of 6mA in metazoans remain controversial and the role of TET in 6mA oxidation is unexpected.

Here, we re-evaluated 6mA presence as well as TET function and mode of action in drosophila. Using a combination of biochemical, genetics and genomics approaches, we show that TET is not involved in 6mA erasure and controls gene expression and fly development essentially in a catalytic-independent manner.

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