

Title: Development of chemical biology toolbox to investigate epigenetic regulation of writers, readers and erasers of 5-methylcytosine

5-methylcytosine (5mC) is a central epigenetic mark of mammalian genome playing important roles in development, differentiation and cancer. Dynamic regulation of 5mC is governed by highly conserved readers, writers and eraser enzymes. 5-methyl mark is deposited by writer enzymes DNA methyltransferases (DNMTs) on cytosine nucleobase of DNA. 5mC in DNA is read by reader proteins like MBDs and MeCP2 leading to gene silencing. Iterative oxidation of 5mC to 5-hydroxymethyl-, 5-formyl-, and 5-carboxylcytosine (5hmC, 5fC, and 5caC) is catalysed by Ten-eleven-translocation (TET) dioxygenases in an iron-, oxygen-, and α -ketoglutarate-(α KG)-dependent fashion. These oxidised nucleobases are not only intermediates of TET oxidation, but also possess inherent regulatory functions via specific interactions with key nuclear proteins, and influence nucleosome stability and positioning. I will discuss the development of various chemical biology tools to modulate the activity of writers, readers and eraser enzymes, which enable deeper understanding of epigenetic regulation of 5mC both in vitro and in vivo