Donnelly Centre
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Zhang Lab Seminar Announcement

"messenger RNA methylation: role in mammalian development"

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Donnelly Centre, Yip / Friesen Red Seminar Room
160 College Street, Toronto

Abstract: In mammals, messenger RNA (mRNA) contains both cap and internal modifications. The most abundant internal RNA modification is covalent linkage of a methyl group to the RNA adenine at N6 position (N6-methyladenosine or m6A). Research in my lab focuses on understanding the functional roles of m6A mRNA methylation in development and disease, as well as the underlying mechanism. Previously, we discovered a heterodimer, consisting of methyltransferase-like 3 (Mettl3) and Mettl14, as mammalian m6A methyltransferase. By manipulating these enzymes in mouse embryonic stem cells, we reported the requirement of m6A in keeping embryonic stem cells at ground state through destabilizing developmental regulators, suggesting an essential role of m6A in early development. Indeed, our recent in vivo analysis revealed that Mettl14 total knockout mice displayed embryonic lethality at peri-implantation stage. To further understand the functional significance of m6A in tissue development, we deleted Mettl14 in embryonic neural stem cells. Cellular analysis suggests that m6A robustly promotes neural stem cell proliferation and enhances neural stem cell self-renewal. Mouse brain lacking Mettl14 displayed decreased neural stem cell pool that led to decreased number of neurons during cortical neurogenesis and an overall reduction in cortical thickness. We are currently investigating molecular mechanisms underlying observed phenotypes. Intrigued by the marked effect of m6A on neural stem cell proliferation, we are also exploring the role of m6A modification in brain tumors. Through these studies, we hope to move forward our understanding on the impact of RNA modification on human health and disease.

Host: Zhaolei Zhang

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