



ON-SITE BIOLOGY COLLOQUIUM

Friday, 17 Nov 2023 | 4 pm | LT32

Hosted by Assist. Prof Tan Yong Zi

Map to Block S1A



Identifying and exploiting nucleic acid modifying enzymes: RNA methylation, CRISPR-Cas, and beyond

By **Leslie Beh**

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About the Speaker

Leslie earned an A.B. in Biology at Harvard University as a John Harvard scholar, and an A.M. and Ph.D. in Biology from Princeton University with Laura Landweber and Tom Muir as a Petrie fellow, where he used genomics and biochemical fractionation approaches to identify a novel DNA methyltransferase complex that is homologous to the RNA m6A methyltransferase, METTL3-14 (Beh et al., Cell 2019). Leslie then embarked on a short postdoctoral stint with Sam Sternberg at Columbia University, where he used genomic, structural, and biochemical approaches to study CRISPR-Cas systems that mediate RNA-guided DNA integration (Hoffmann*, Kim*, Beh* et al., Nature 2022, *co-first authors). Following this, Leslie pursued a career in industry, joining Illumina to lead a research group for developing novel epigenetics assays. Driven by the desire to do biological research and make an impact on students, Leslie returned to A*STAR / IMCB in September 2022 as a Principal Investigator.

The natural world harbours a vast diversity of enzymes, many of which remain uncharacterised. My research focuses on discovering novel DNA and RNA modifying enzymes, dissecting their mechanistic basis of function, and repurposing them for biotechnological applications. Here, I describe three efforts in this theme: 1) the discovery of a eukaryotic DNA N6-adenine (m6A) methyltransferase and its evolutionary links with the canonical m6A RNA methyltransferase, METTL3-14; 2) engineering m6A-modifying enzymes to understand the biological function of m6A and its impact on immunogenicity; 3) the discovery of a transposon-encoded CRISPR-Cas system that mediates programmable RNA-guided DNA integration, and its applications in gene therapy.