NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

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Hosted by Prof Gong Zhiyuan

Translating a CRISPR discovery into innovative diagnostics for infectious diseases

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Traditional diagnostic tools are inadequate for detecting and responding to pandemics and complex chronic diseases. CRISPR, the adaptive immune system in prokaryotes, is a never-ending source of new technologies, offering fresh solutions. Here, we convert a CRISPR discovery into innovative RNA detection and recording platforms for disease diagnosis. We found that tracrRNA, which facilitates CRISPR RNA processing and maturation within CRISPR-Cas9 systems, can also mediate the generation of non-canonical CRISPR RNAs (ncrRNAs) derived from host cellular transcripts. Our ncrRNA discovery inspired the engineering of reprogrammed tracrRNAs (Rptrs) that link the presence of any RNA-of-interest to DNA targeting with different Cas9 orthologs, creating a multiplexable diagnostic platform termed LEOPARD (Leveraging Engineered tracrRNAs and On-target DNAs for Parallel RNA Detection). We extended tracrRNA reprogramming to diverse dsDNA-targeting Cas12 nucleases, resulting in PUMA platform (Programmable tracrRNAs Unlock protospacer-adjacent Motif-independent detection of ribonucleic Acids by Cas12 nucleases). Finally, we applied the concept of Rptr from in vitro to the cellular context, and established a user-defined RNA recording platform TIGER (Transcribed RNAs Inferred by Genetically Encoded Records), addressing the challenge of recording transcriptional history events at the single-cell level.

About the Speaker

Chunlei completed his MSc in Microbiology at Shandong University in China in July 2015. He used comparative genome analysis to decipher the genetic variations and underlying molecular mechanisms in a highly efficient xylose-fermenting strain of yeast. He then worked as a Project Engineer in Singapore, applying CRISPR-based tools to engineer yeast. Chunlei joined the Beisel lab at the Helmholtz Institute for RNA-based Infection Research (HIRI) in Germany as a PhD student in 2018. As part of his PhD study, he developed a reprogrammed tracrRNA-based CRISPR technology for multiplexed diagnostics. Starting in 2022, he continued his research as a postdoc in the same group to apply the technology to other CRISPR systems and cellular settings for disease diagnosis.