NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

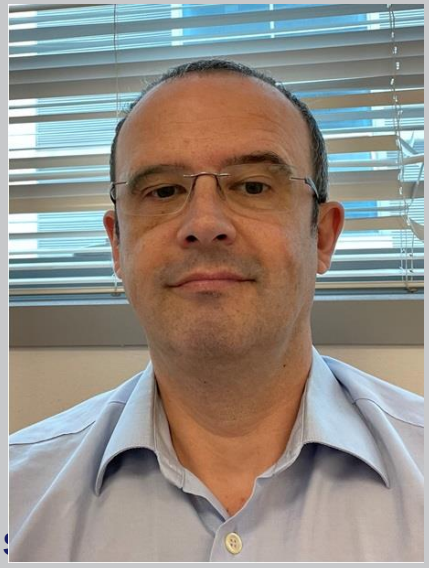
SRRM2 organizes splicing condensates to regulate alternative splicing in human myeloid cells

Date: **15 January 2021, Friday**

Time: **4pm**

Venue: **Classroom 1, SBS**

Our lab studies splicing mechanisms and their implications in human genetic diseases including cancer. As a major research line, we recently profiled alternative splicing in human myeloid cells such as monocytes/macrophages and neutrophils. In this seminar, I will present one subproject centered on the SRRM2 splicing factor, which we identified as a key player in human myeloid cells, likely both in physiology and leukemia. SRRM2 was known as a nuclear speckle marker containing multiple disordered domains, and we now show that it forms biomolecular condensates in human cells with hallmarks of liquid-liquid phase separation. By live-cell imaging, we found that SRRM2 is responsible for organizing nuclear speckles through cell cycle. Our transcriptomic data in THP-1 monocyte-like cells show that SRRM2 deficiency mainly induces skipping of cassette exons with specific properties, and that it acts co-transcriptionally. Functionally, SRRM2 regulates several splicing events important for myeloid cells, including production of a FES splice isoform that attenuates innate inflammatory responses. Our long-term goal is to connect SRRM2 condensate formation with splicing regulation and cellular function. Our results reveal that SRRM2 acts as a scaffold to organize nuclear speckles likely via phase separation, which in turn regulates alternative splicing in innate immunity.



Francesc Xavier Roca Castella
Associate Professor
School of Biological Sciences
Nanyang Technological University