NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Chromatin scrunching by human architectural factor HMGA2 to safeguard the genome

Date: **28 August 2020, Friday**

Time: **4pm**

Venue: **Classroom 1, SBS**

The high mobility group AT-hook 2 (HMGA2) protein is an oncofetal factor normally expressed only during early developmental stages and aberrantly re-expressed in many highly aggressive cancers. The protein plays an important context-dependent role in the regulation of gene expression by modulating chromatin structure and thereby promoting cell proliferation and differentiation. Recently, we and others have provided evidence that HMGA2 is also implicated in maintenance of genome stability, in particular DNA repair. Furthermore, my group has identified a novel function of HMGA2 as DNA replication fork chaperone in stem and cancer (stem) cells. Fork chaperoning contributes to genome stability by attenuating replication fork collapse into double strand breaks during natural or induced replication stress thereby reducing cell death. Here, I will summarize our multi-disciplinary approach to elucidate the mechanism underlying replication fork chaperoning, which suggests that HMGA2-mediated scrunching and constrainment of (+) chromatin supercoiling in combination with stimulation of DNA topoisomerase II are critical. Since this novel function of HMGA2 protects cancer cells from the onslaught of several clinically highly relevant chemotherapeutic drugs that induce fork collapse, we screened for HMGA2 antagonists using our own cell-based high throughput compound assay. This resulted in a number of hits that are currently being investigated.

Speaker:

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