

CSCB Hybrid Seminar Series

The Nuclear LINC Complex as a Therapeutic Target for Treating striated Muscle Disease and Cardiomyopathy.

Date: 14th September 2021 (Tuesday)

Time: 12noon-1pm (SGT)

Venue:

Zoom details:

<https://nus-sg.zoom.us/j/88155613013>

Meeting ID: 881 5561 3013

Passcode: 668302

Talk venue (attendance by registration only):

Amphitheatre, Level 2, Duke-NUS Medical School

Abstract:

Many diseases, including dilated cardiomyopathy (DCM), muscular dystrophies, lipodystrophy and progeria are caused by mutations in the A-type lamins (LMNA) and other NE proteins. The lamins comprise the nuclear lamina, maintain nuclear shape and tether the nucleus to the cytoskeleton through the NE associated LINC complex, so providing a direct physical link between the cell surface/ECM and nucleoplasm. The LINC complex protein Sun1 and its N-terminus protrudes into the nucleoplasm where it interacts with nuclear proteins. In differentiating myoblasts, a muscle specific isoform of SUN1 interacts with the microprocessor enzyme DROSHA. SUN1 inhibits the processing of a cluster of microRNAs that regulate the translation of RTL1, a protein required for efficient skeletal muscle regeneration. Many of the Lmna mutations result in elevated levels of Sun1. Deleting Sun1 in mice that rapidly die from Lmna induced heart failure results in their survival for more than 1 year, identifying a therapeutic route to treating DCM. We developed a dominant negative Sun1 minigene that on introduction into DCM hearts significantly ameliorates many of the Lmna induced cardiac muscle pathologies.

Speaker:



Colin Stewart

Professor

A*STAR Skin Research Laboratories

Agency for Science, Technology and Research (A*STAR)

Colin Stewart has pioneered the development of many techniques, now widely used in mouse experimental genetics, and establishing protocols for deriving embryonic stem (ES) cells, including the first human ES and uniparental ES lines. He identified the cytokine LIF as being crucial to sustaining stem cell pluripotency and that LIF is essential in regulating uterine receptivity for embryo implantation. His interests now centre on the laminopathies, a heterogeneous collection of diseases arising from mutations in the LaminA gene. With Nicolas Levy he identified mutations in the LMNA gene causing progeria, and has developed mouse and iPS models of this disease. Currently and as a founding member of Nuevocor, he is developing new therapeutics to ameliorate dilated cardiomyopathy and vascular disease.

Host:

David Virshup

Professor & Director

Programme in Cancer & Stem Cell Biology

Duke-NUS Medical School

Singapore

No registration is required for attendance via Zoom.

All are welcome.