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

BIOLOGY COLLOQUIUM

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Hosted by A/P Ge Ruowen

Functional Architecture of the Cell's Nucleus in Development, Ageing and Disease

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The nuclear envelope (NE) and lamina are the boundary between the cells nucleus and cytoplasm. Some 25 diseases have been mapped to genes encoding proteins of the lamina and NE. Half these diseases, which include muscular dystrophies, cardiomyopathies, lipodystrophy, skeletal dysplasia and the premature ageing disease, Progeria, are caused by mutations in the A-type lamins. The A-type lamins are the principal components of the nuclear lamina. The lamina provides both mechanical strength and shape to the nucleus, and functions as a scaffold for other nuclear proteins regulating chromatin organization, DNA replication and transcription.

We find the composition of the cells nuclear envelope and lamina changes during embryogenesis and shows tissue specific differences. We have investigated how the lamina and NE is required to regulate heterochromatin organization during development. In addition, we have found that components of the LINC complex that connects the cytoplasmic cytoskeleton to the interphase nuclear machinery at the NE and lamina, shows tissue specific differences. As examples, 2 members of the LINC complex, the KASH domain proteins KASH4 and 5 show restricted expression to the cochlear hair-cell nuclei and primary spermatocytes respectively. Whereas KASH4 is important for maintaining nuclear position in the outer hair cells, KASH5 is important in mediating chromosome pairing and movement during "bouquet" formation, an essential component of meiosis throughout the animal kingdom.

Overall the structure of the cells interphase nucleus is increasingly relevant to understanding function of some key tissues, and when this structure is disrupted this leads to different diseases.

Artwork by Ann Nee, DBS, NUS