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

BIOLOGY COLLOQUIUM

Friday, 6 Nov 2015 | 4pm | DBS Conference Room 1

Hosted by Dr Lu Gan

Structure and Dynamics of Nucleosome Interactions in the Chromatin Fibre



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Genomic DNA in the eukaryotic cell nucleus is highly condensed into chromatin. The positively charged N-terminal histone tails mediates this compaction. Access to DNA during transcription, replication and repair requires decondensation of chromatin. The histone tails are subject to a range of posttranslational modifications, one being acetylation of lysines, which regulates chromatin compaction. Understanding the mechanisms of the chromatin folding through covalent modifications of the histone N-terminal tails is hampered by a lack of accessible in vitro reconstituted chromatin containing precisely modified histones. We developed methods for preparations of large quantities of histones with well-defined tail modifications. A novel direct chemical approach, without ligation chemistry, was recently introduced. We investigated chromatin fibre folding and fibre-fibre self-association (inter array aggregation) of nucleosome arrays containing various combinations of acetylated lysines We found that the single H4-K16 acetylation is sufficient to antagonize array folding while inter-array self-association is unspecifically electrostatically controlled. We used various biophysical methods such as analytical ultracentrifugation, X-ray diffraction (SAXS), NMR, EM and single molecule force spectroscopy (magnetic tweezers). Recently, we have been participating in a major research programme (funded by a MOE Tier 3 grant) to investigate structure and dynamics of telomeric chromatin.

Artwork by Ann Nee, DBS, NUS