Student oral presentation

Session 1

Role of nuclear lamins in the regulation of SIRT6

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Sirtuins are a family of proteins which have been involved in a multitude of biological functions, especially longevity expansion. SIRT6 is a mammalian sirtuin with emerging functions in a spectrum of cellular events, such as cellular senescence, premature aging, DNA damage response, metabolism, extending lifespan and also tumor suppression. Although SIRT6 has been established to regulate a range of cellular functioning, its upstream regulation has remained elusive till date. Given its crucial roles in so many vital processes, identification of its endogenous activators can serve as effective therapeutics. On the other hand, lamin A is a nuclear lamina protein involved in the maintenance of nuclear structure, gene regulation and several other important functions. A point mutation in LMNA gene (encoding lamin A) results in progerin (the mutant isoform of lamin A containing 50 amino acids deletion at the C-terminus), which causes Hutchinson-Gilford Progeria syndrome (HGPS), a severe early onset premature aging syndrome. In my study, I have identified lamin A as the endogenous activator of SIRT6 towards histone deacetylation and also DNA double-strand break repair. Intriguingly, progerin exhibited impaired activation towards SIRT6 functioning. To understand the biological significance of this observation, we investigated SIRT6 functioning in fibroblasts derived from HGPS patients. Interestingly, HGPS fibroblasts also displayed impairment in SIRT6-mediated DNA damage repair process, thus indicating that impaired SIRT6 functioning is another defective mechanism resulting in progeria.

Dust Mite & Allergy: Multi-omic Approach Reveals a Broad Spectrum of Allergens

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(Supervisor: Professor TF Chan, CUHK)

House dust mite (HDM) is the most pervasive inhalant allergen source worldwide, with over 50% of allergic disease cases being attributed to them. Allergens derived from HDM are associated with sensitization and asthma, and it affects people of all ages. It is estimated by the World Health Organisation that 300 million individuals were affected with asthma in 2011, and approximately 250,000 people die prematurely each year from asthma. It is therefore important to have a comprehensive study on HDM to advance our understanding of HDM allergens. In 1920s and 30s, it was thought that HDM contained only a single allergen; it was until 1969, Voorhost et al. reported that HDM indeed harbored a mixture of allergens. In 1970s, Halmai and Alexander further isolated faecal pellets from the bodies of mites and performed skin-prick tests to demonstrate their allergenicity. With decades of effort, the functions of 23 HDM allergen groups have been revealed, yet the full spectrum of HDM allergenic components remains incomplete. In this study, we have isolated Dermatophagoides farinae (D. farinae) – the dominating HDM in southeastern China, and performed both DNA and RNA sequencing to assemble the draft genome & transcriptome. In addition to genome assembly, 112k genomic sequencing reads were able to map uniquely to a list of microbial species, hence determining the microbiome of D. farinae. Cross-comparison between D. farinae and other mite species such as spider mite & predatory mite also reveals the particularly broad spectrum of allergen genes harbored in D. farinae. It is believed that this work can be used as a future investigative tool for identification and characterization of HDM allergens.