NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Seminar Announcement

AKTIP (Ft1), a telomeric protein that interacts with lamin, is required for mouse survival and development

Date: 29 June 2015 Monday

Time: 3:00pm to 4:00pm

Venue: SBS Classroom 2 (SBS-01n-22)

Host: A/Prof Peter Dröge

Speaker: Prof Isabella Saggio
Genetics and Gene Therapy
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Abstract

We have identified a new telomeric accessory protein named AKTIP, Ft1 in mouse, an ubiquitin E2 variant enzyme, which interacts with TRF1 and TRF2 and immunoprecipitates telomeric DNA. Loss of Ft1 results in fragile telomeres and sister telomere associations. In doubly depleted TRF1/Ft1 cells, the TRF1-induced fragile telomere phenotype is epistatic to that of Ft1, suggesting that TRF1 and Ft1 are involved in a common molecular pathway, likely telomere replication. In line with this hypothesis, we observed that AKTIP interacts with the DNA replication factors PCNA and RPA70, and, in AKTIP depleted cells, telomeric replication is impaired. A further feature of AKTIP that we have more recently investigated is its interaction with lamins. LaminA/C and lamin B1 were identified by mass spectrometry analysis in AKTIP-enriched protein extracts. AKTIP co-localizes with lamin B1 at the nuclear lamina and co-immunoprecipitates lamin A/C and lamin B1. The expression of the premature aging-related mutated lamin A, named progerin, results in AKTIP delocalization from the nuclear rim. Interestingly, AKTIP depletion causes the selective reduction of lamin A, but not of lamin B1 and lamin C. Fifteen days upon AKTIP depletion, primary cells show distorted nuclei and senescence-associated markers, which recalls the phenotype of progeroid cells. In vivo, the depletion of the Ft1 causes premature death and severe abnormalities, including the absence of subcutaneous fat, skeletal and muscle alterations and male sterility. Altogether, our results suggest that the telomeric protein AKTIP/Ft1 plays a crucial role in vitro and in vivo, which intercepts that of lamins.