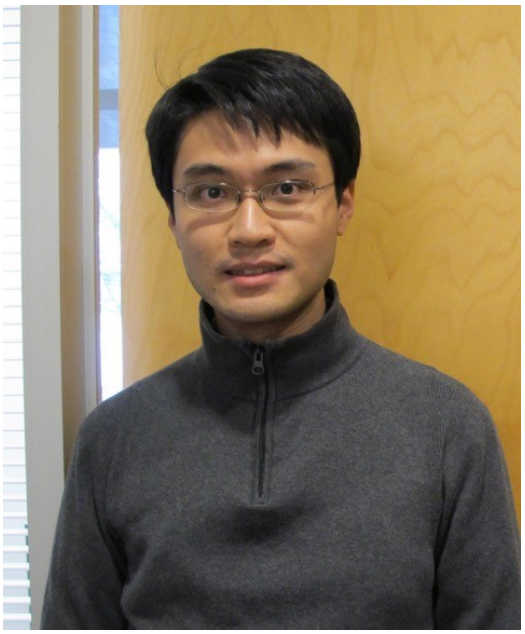
The Centre for Blood Research Seminar Series



Wednesday, January 24, 2018

LSC 3 | 12:00 - 1:00PM

Dr. Calvin Yip

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"Molecular architecture of the enigmatic Elongator complex"

Evolutionarily conserved from yeast to humans, Elongator is a ~850kDa, 6-subunit protein complex originally isolated as a component of the elongating form of RNA polymerase II. However, more recent studies suggest that this complex plays an important role in translation regulation by mediating the modification of transfer RNAs (tRNAs), specifically the addition of 5-methyoxycarbonylmethyl and 5-carbamoylmethyl to the wobble base pair that stabilizes codon-anticodon interactions. Deficiencies in human Elongator give rise to serious pathological conditions, most notably a rare genetic disease known as Familial Dysautonomia (FD). In this seminar, I will present our recent work on characterizing the molecular structure of this enigmatic complex. Using single-particle electron microscopy (EM), our group revealed that Elongator from yeast Saccharomyces cerevisiae adopts a bilobal architecture and an unexpected asymmetric subunit arrangement. By integrating our EM data with available subunit crystal structures and restraints generated from cross-linking coupled to mass spectrometry, we constructed a multiscale molecular model of yeast Elongator. This model showed that two copies of the main catalytic subunit Elp3 are located in distinct environments, a finding that this might explain the basis of Elongator's multifunctionality. Finally, our model confirms the importance of the C-terminal domain of the Elp1 subunit in mediating complex dimerization, and generates the foundation for further understanding the molecular etiology of FD.

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