Tata Institute of Fundamental Research
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Seminar

Cell-type specificity of septin cytoskeleton – what we learnt from the Sept7 knockout model

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Septins are evolutionarily conserved cytoskeletal proteins with well-established role in cell division, especially in the process of cytokinesis. With the emergence of diverse non-canonical functions ranging from neuronal morphogenesis to antibacterial immunity, septins are gaining prominence as a distinct fourth component of the mammalian cytoskeleton (Mostowy and Cossart 2012; Menon and Gaestel 2017). SEPT7 is the unique member of the mammalian septin family which is a core and irreplaceable component of septin filaments. This vital role is reconfirmed by the early embryonic lethality observed in the Sept7$^{-/-}$ mice and the obligate multinucleation associated with Sept7-deleted fibroblasts (Menon et al. 2014). But interestingly, Sept7 deletion in the hematopoietic compartments does not lead to any developmental defects, despite the co-depletion of the other core septin proteins. Hence, cell-type-specific mechanisms must exist that compensate for the lack of septins in the immune cells. However, the differential role of septins in mammalian cytokinesis could open novel therapeutic windows, where specific targeting of septins could help in anti-tumor therapy with minimum effects on hematopoiesis (Menon and Gaestel 2015). Research using a Sept7$^{-/-}$ fibroblast rescue model could discover the dispensability of the SEPT7-dimerisation in fibroblast division, highlighting SEPT7-SEPT9 or SEPT9-SEPT9 interfaces in the filaments as possible targets for pharmacological intervention (Abbey et al. 2016). While hematopoiesis in general is not affected in the absence of septins, there seems to be a context and stimulus dependent role for septins in the immune response. Future studies aimed at the identification of small molecule modulators of septin cytoskeleton, cell-type specific septin-interactomes and non-canonical septin functions in the immune system will be necessary to fully understand the cell-type specificity of septin functions.

Tuesday, May 29th 2018

4:00 PM (Tea/Coffee at 3:30 PM)

Auditorium, TIFR-H