

MBG FOCUS TALK

Hosted by Esben Lorentzen

Monday 29 April 2024 at 10:00

Faculty Club (1870-816)



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Hyperactive Protein Responses and Functional Residuomics of Cilia

My seminar addresses the complex mechanisms by which cells regulate hyperactive ciliary proteins. Our recent research has revealed a novel role of RNA editing in controlling hyperactive ciliary kinases. By editing the mRNA of the hyperactive kinases themselves, this process effectively reduces kinase translation, thereby mitigating hyperactivity (Li et al., Science, 2021). Additionally, we have uncovered a fascinating pathway in sensory neurons, wherein hyperactive intraflagellar transport (IFT) kinesin is expelled and subsequently cleared by surrounding glia cells. Intriguingly, the fate of this kinesin is determined by its conformation and activity level. These discoveries collectively illustrate that living cells deploy multiple, previously unanticipated strategies to cope with hyperactive proteins. Furthermore, our findings suggest that perturbations at distinct amino acids within a protein can trigger different cellular responses, underscoring the emerging area of functional residuomics which provides residue-precise functional knowledge of the proteomic landscape. We propose that the use of artificial evolution methodologies, combining systematic chemical mutagenesis, genetic screens, and whole-genome sequencing, can advance our knowledge in functional residuomics.