

Students' Annual Seminar

Structure of G57W variant of human γ S-crystallin and its involvement in severe infantile cataracts

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A recently identified G57W variant of human γ S-crystallin is associated with dominant infantile cataracts, the familial determinate of childhood blindness worldwide [1]. To investigate the structural and functional changes that compromise eye lens transparency and cause lens opacification, we determined the high resolution 3D structure of human γ S-G57W [2] and studied its conformational dynamics in comparison to its wild-type [3] by solution NMR spectroscopy. Consistent with differential domain dynamics, our results from H/D exchange NMR spectroscopy show sequential deprotection of foldons indicating presence of partially unfolded intermediates [4]. Site-specific conformational ruggedness is quantified from non-linear dependences of amide proton chemical shifts in human γ S-G57W upon thermal agitation [5]. Overall, this study provides a residue resolved understanding of the structure-function paradigm as one shifts from physiology to pathology with critical therapeutic consequences.

References:

- [1] K. J. Bari et al., 2018. *Biomol NMR Assign* 12(1), 51-55.
- [2] K. J. Bari et al., 2019. *J. Struct. Biol.* 205(3), 72-78.
- [3] K. J. Bari et al., 2019. *Biochem. Biophys. Res. Commun.* 511(3), 679-684.
- [4] K. J. Bari et al., 2019. *Biochem. Biophys. Res. Commun.* (in press).
- [5] K. J. Bari et al., 2019. *Biochem. Biophys. Res. Commun.* (in press).

Friday, May 10th 2019

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

Seminar Hall, TIFR-H