

## Catalytic Amyloid Based Materials as the Earliest Protein Fold?

Akhil Venugopal, Mahesh Yenuganti and Dibyendu Das\*

\*Email: [dasd@iiserkol.ac.in](mailto:dasd@iiserkol.ac.in)

Recently, our lab is interested in understanding how the biopolymer evolution happened, especially from the perspective of proteins?<sup>1-4</sup> In this context, extant proteins, evolved over millions of years, carry out an impressive array of responsibilities, from catalysis and molecular recognition to motility and compartmentalization. But there remain critical gaps in our understanding of how evolution of proteins happened. Any standard small protein is at least 100 amino acids long with molecular weight starting from 10,000 Da. How Nature stumbled upon the sequence of extant protein, from the astronomical pool of sequences is still an open question. Towards this end, we propose that short amyloids capable of assembling in harsh conditions, with specifically ordered paracrystalline structures<sup>2-4</sup> might have been the earliest protein folds. Our recent results demonstrate self-assembled short peptide can act as surrogates to the long polypeptide chains of extant peroxidases. Further, we show two important chemical transformations associated with extant enzymes like esterases and peroxidases were targeted and simultaneously accomplished by minimal short amyloid based nanostructures, and thus setting the stage for amyloids as the earliest protein folds. Looking beyond, materials derived from these short peptides can be used for non-aqueous enzymology relevant for pharmaceutical industries.<sup>2</sup>

### References:

1. Harish, A.; Caetano-Anolles, G. *PLOS ONE* **2012**, *7*, e32776.
2. Kapil, N.; Singh, A.; Das, D. *Angew. Chem. Int. Ed.* **2015**, *54*, 6492–6495.
3. Kapil, N.; Singh, A.; Singh, M.; Das, D. *Angew. Chem. Int. Ed.* **2016**, *55*, 7772-7776.
4. Singh, A.; Kapil, N.; Mahesh, Y.; Das, D. *Chem. Commun.* **2016**, *52*, 14043-14046.