Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Seminar

Genetics of aging and age-related disorders in zebrafish

Ajeet Pratap Singh

Novartis Institutes for BioMedical Research, Cambridge, USA

Aging is considered as the major risk factor for multiple disorders including cognitive decline, neurodegeneration, cardiovascular disease, kidney disease, decline in immune system, and cancer. It is therefore of interest to develop a basic understanding of the core mechanisms underlying aging in order to identify novel targets for preventing or slowing down age-related conditions. Using genetic, genomic and imaging based methods in zebrafish, we are attempting to understand fundamental mechanisms underlying aging and age-related disorders. We will discuss our ongoing work in general, and focus on α-Klotho pathway in particular. The hormone α-Klotho regulates mineral homeostasis and plays a key role in linking mineral homeostasis to aging in mammals. α-Klotho levels decline with age in humans and its deletion in mice severely shortens lifespan, while mice overexpressing α-klotho live longer. However, mechanisms underlying mineral homeostasis have evolved to serve environmental needs, and differ dramatically between animals living in different habitat. We investigated the role of α-klotho in zebrafish, a vertebrate with a distinct mineral metabolism. Mutations in α-klotho, and fibroblast growth factor-23, its binding partner reduce lifespan, with abrupt onset of behavioral and degenerative physical changes in adulthood. There is widespread calcification of vessels, most dramatically in the outflow tract of the heart, the bulbus arteriosus. This calcification is associated with ectopic activation of pathways involved in remodeling of bone and extracellular matrix, and of osteoclast differentiation. We will discuss this work in the context of aging, and elaborate on our ongoing efforts to build a framework to study organismal aging for target discovery.

Monday, Apr 15th 2019

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

Seminar Hall, TIFR-H