RCB-Colloquium

Thursday, November 27, 2025 – 14:00 h

H 53

Prof. Dr. Andreas Neueder

Center for Molecular Neurobiology (ZMNH)
University Medical Center Hamburg-Eppendorf

RNA Biology and HTT Fragment Generation by Incomplete Splicing in Huntington Disease

Expansions of microsatellites, repetitive nucleotide sequences scattered throughout the genome, are the cause of a number of diseases. **Huntington disease (HD)** is the most common disease of a family of disorders that is caused by expansions of a CAG triplet sequence in their coding region. **Huntingtin** (HTT), the gene harbouring the **expanded CAG repeat** in HD, is a ubiquitously expressed, and alternatively spliced gene that gives rise to several canonical and numerous disease related isoforms. Alternative splicing of the HTT gene and proteolytic cleavage of the HTT protein generate C-terminally truncated fragments of HTT. The **severity of disease** and molecular phenotypes is strongly correlated with **smaller N-terminal fragments**. The **most toxic fragment of HTT** is **encoded by exon 1**, which includes the expanded CAG tract, and induces both protein and RNA based toxicity. We have shown that this fragment is translated from a novel, disease-related isoform of HTT, **HTT1a**, that is generated by a **block in the splicing of exon 1 to exon 2.**

Host: Fachschaft Biologie Regensburg
Fachschaft.Biologie@biologie.uni-regensburg.de

Universität Regensburg
Biochemie-Zentrum Regensburg