

SEMINAR

Who: Dr. Luca Ferrari
Max Perutz Labs
University of Vienna

Host: Dr. Katarzyna M. Grochowska
ZMNH, Hamburg

Title: Reconstituting Proteostasis Failure in Neurodegeneration: From Patient-Derived Aggregates to Mechanism

2026

Tue

Oct.

13th

3 p.m.



Where: ZMNH

Falkenried 94

20251 Hamburg

Big Seminar Room E.82, Ground Floor

Zoom Link: <https://uke-de.zoom-x.de/j/62645757925?pwd=7GZ2pxuelXdtx8IU3D6VmvSHpdVdPw.1>

ABSTRACT:

Our cells use an internal surveillance system, the proteostasis network, to recognise and remove damaged proteins. Yet in Alzheimer's disease, Tau aggregates are recognised by this machinery and still accumulate. Why does recognition fail to become clearance?

I address this paradox using native Tau aggregates purified from postmortem brain tissue of patients with Alzheimer's disease, preserving disease-specific folds and post-translational modifications. A microscopy-based interaction platform I developed makes this challenging

material biochemically tractable, allowing us to dissect how pathological aggregates engage the clearance machinery. In our work (Ferrari et al., Science Advances 2024), we showed that p62 and NBR1 saturate the scarce ubiquitin marks on Tau fibrils, excluding TAX1BP1 and disrupting the assembly of the autophagy machinery.

We are now moving upstream to E3 ubiquitin ligases: which enzymes recognise native Tau aggregates, how do they engage their surfaces, and what determines whether this interaction promotes degradation? Combining patient-derived material, structural mass spectrometry and human neuronal models, we aim to resolve and manipulate these interfaces to turn aggregate recognition into productive clearance.