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**Harm Kampinga**

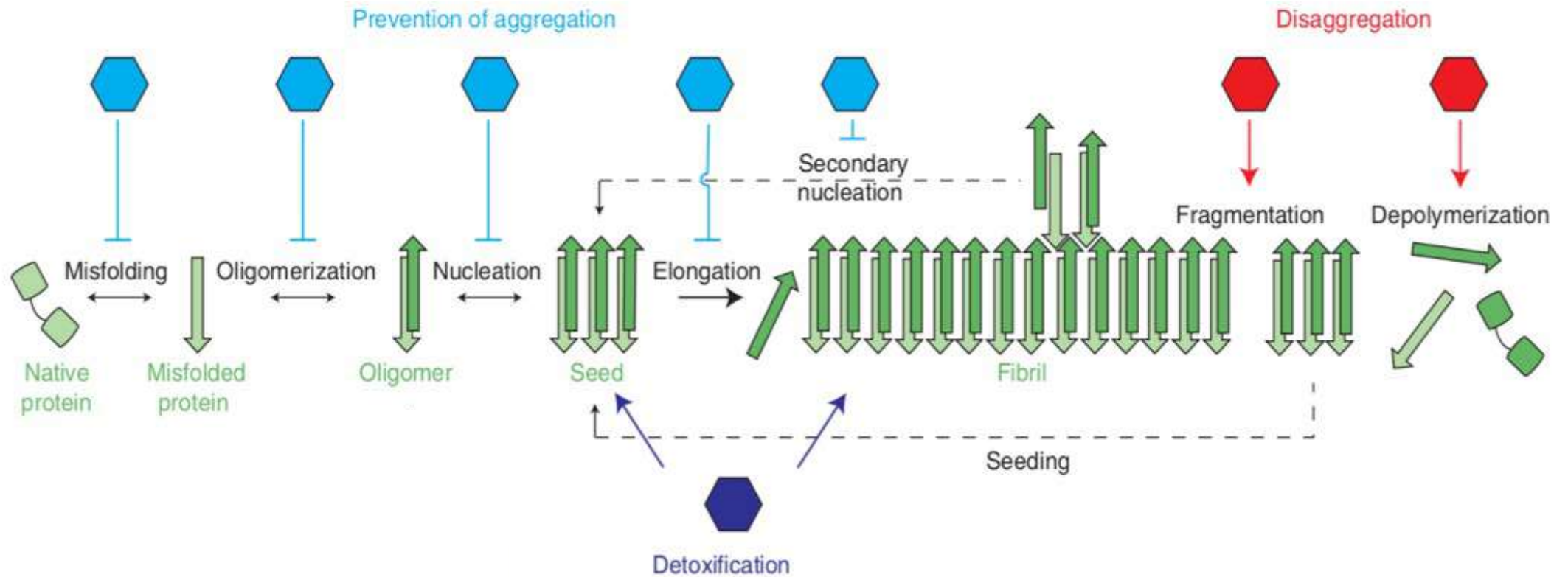
University of Groningen, Netherlands



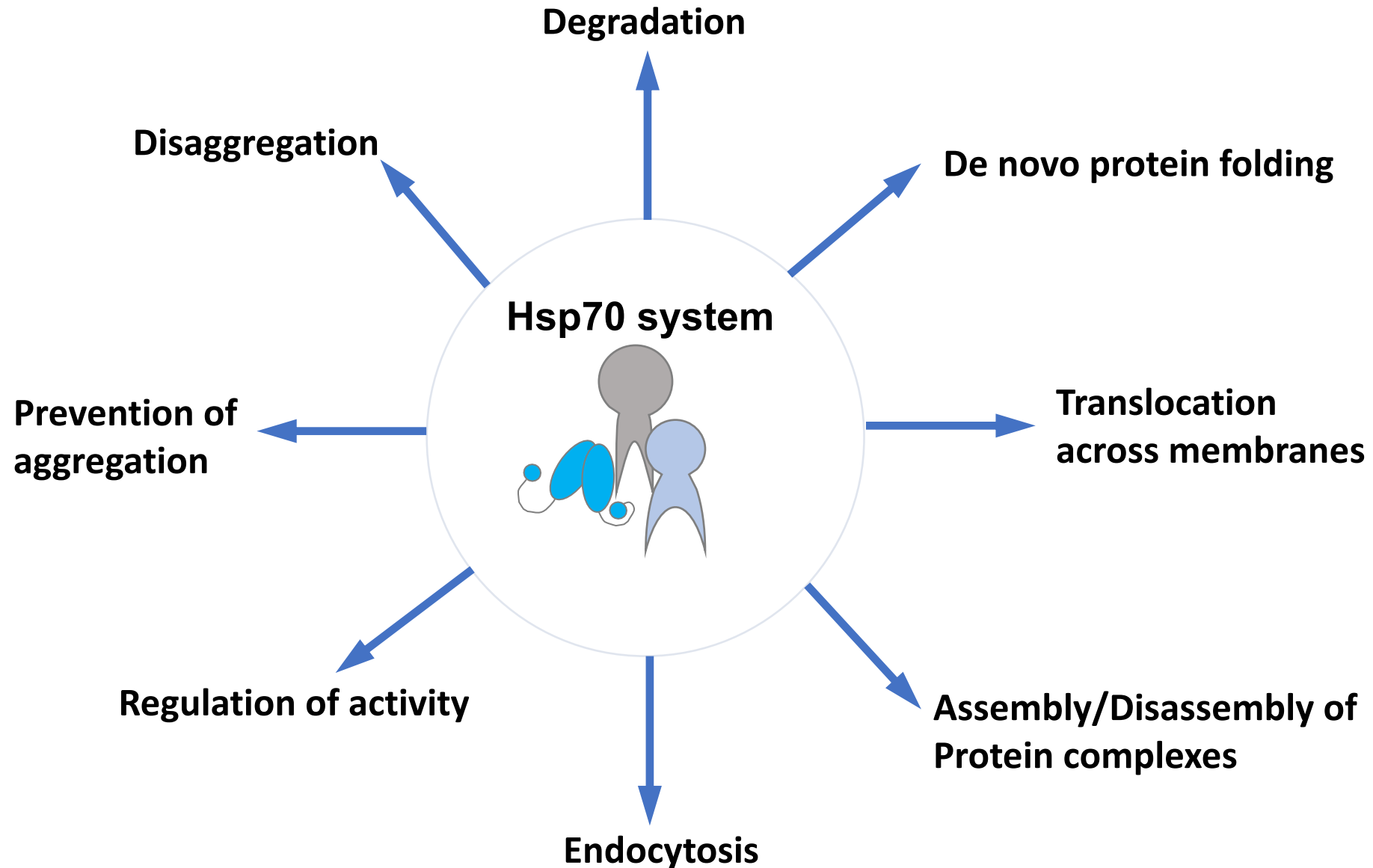
**Christian Hansen**

Lund University, Sweden

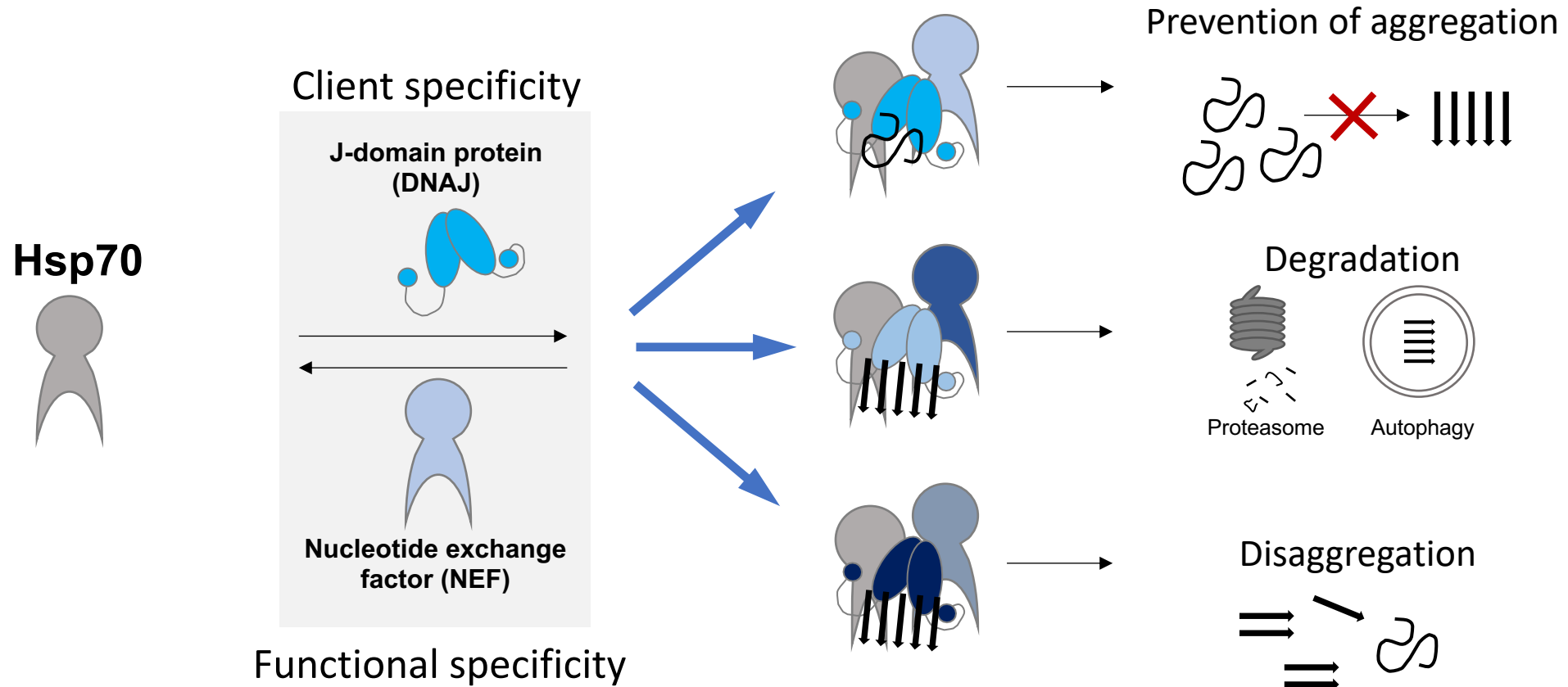
# Molecular chaperones affect the amyloid formation process at multiple steps



# The diverse activities of the Hsp70 chaperone system



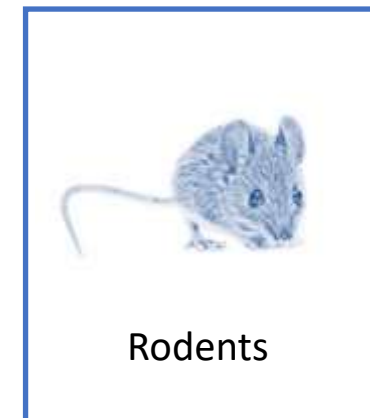
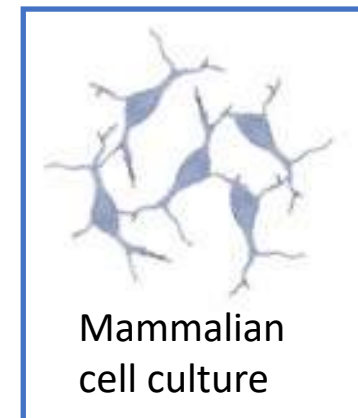
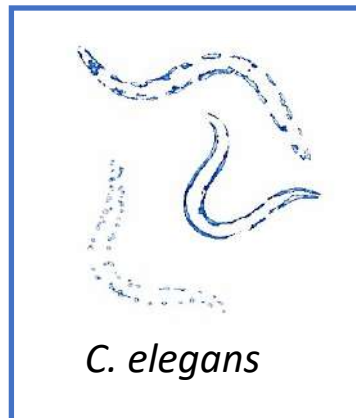
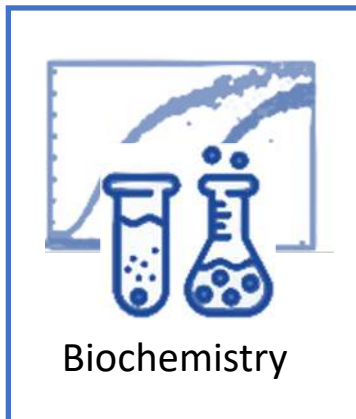
# Hsp70 co-chaperones mediate substrate and functional specificity



➤ **AIM: Identification and characterization of Hsp70 co-chaperones that target  $\alpha$ -Syn and tau**

- *Screen for Hsp70 co-chaperones and determine their mode of action*
- *What is the physiological outcome of their activity?*
- *Effect on structurally distinct assemblies of  $\alpha$ -Syn and tau?*
- *Therapeutic potential?*

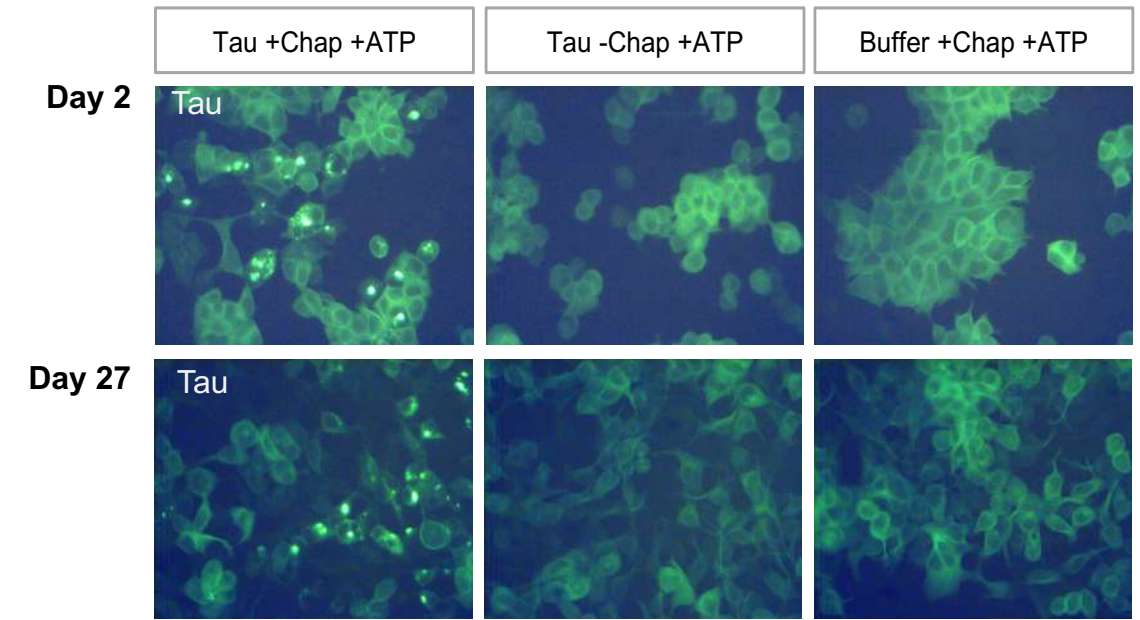
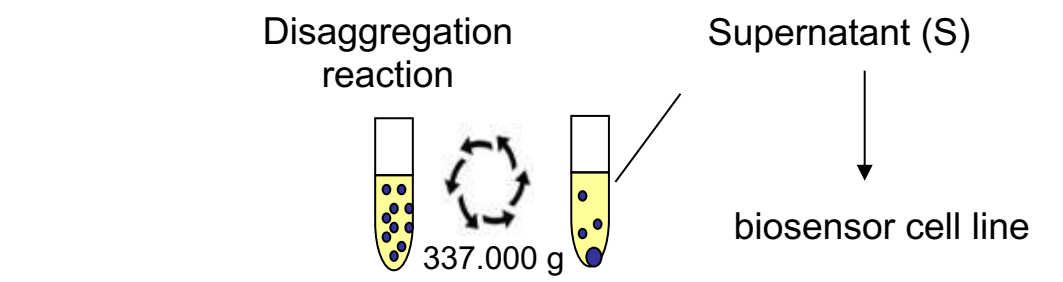
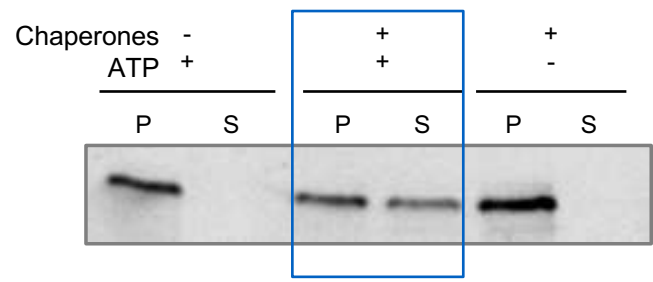
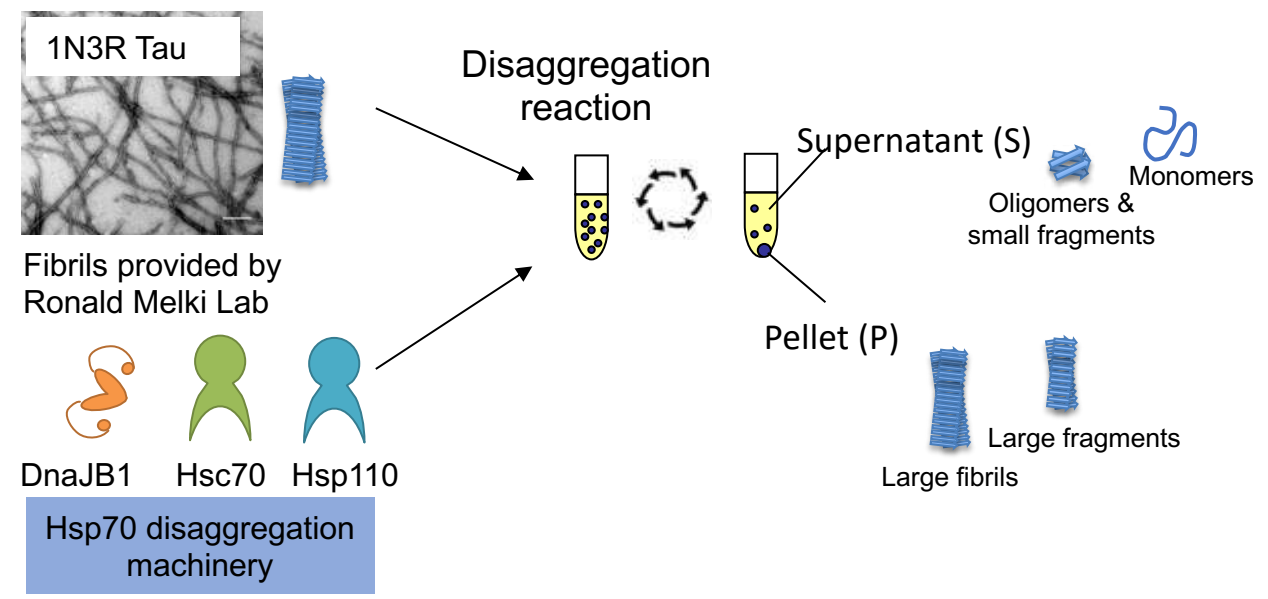
➤ **Model systems:**



# Main Results

➤ Recombinant tau fibrils are disassembled by the Hsp70 disaggregation machinery

➤ Material liberated from tau fibers is able to induce self-propagating aggregates

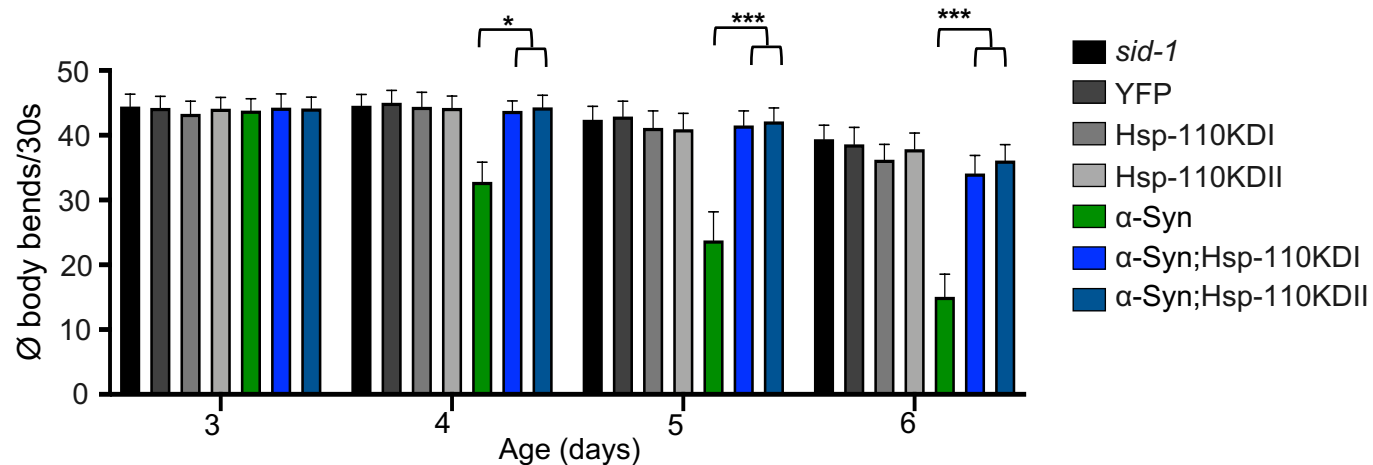
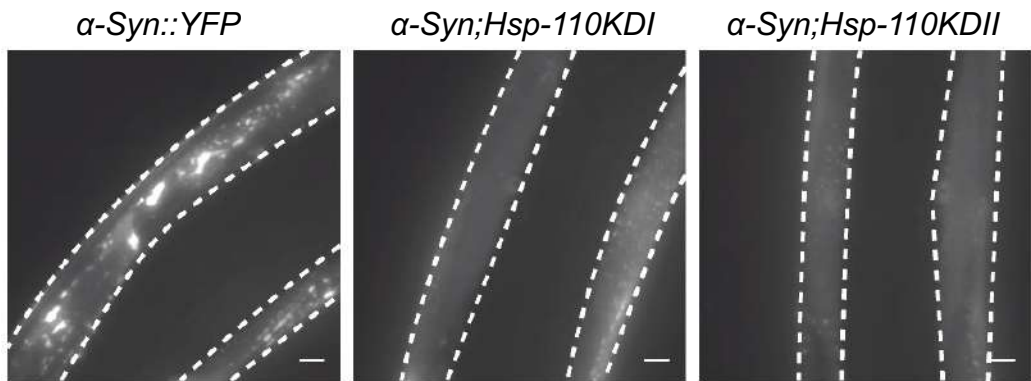


Tau cell line provided by McEwan Lab

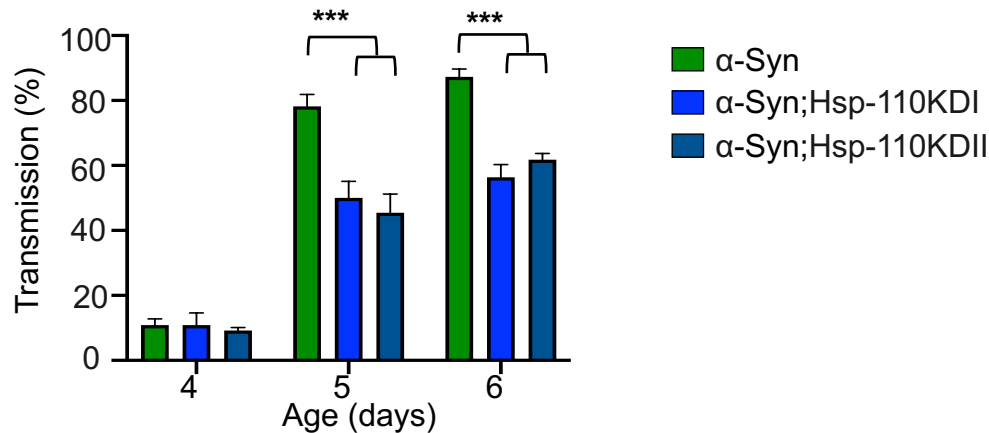
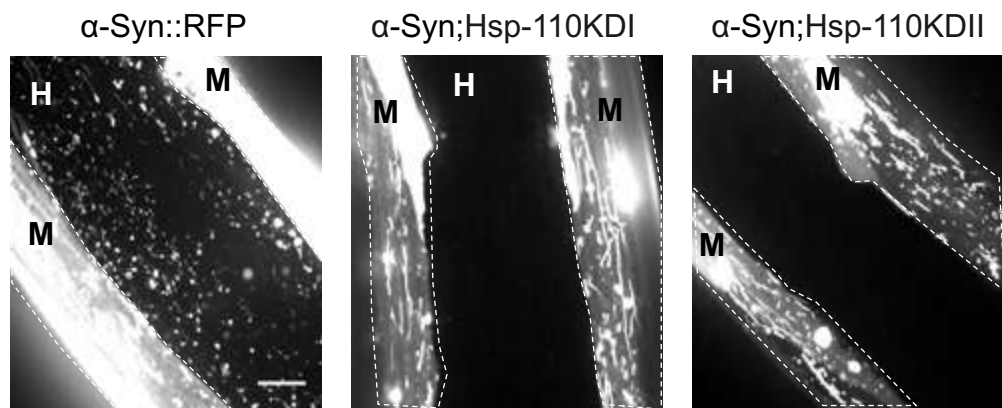
# Main Results



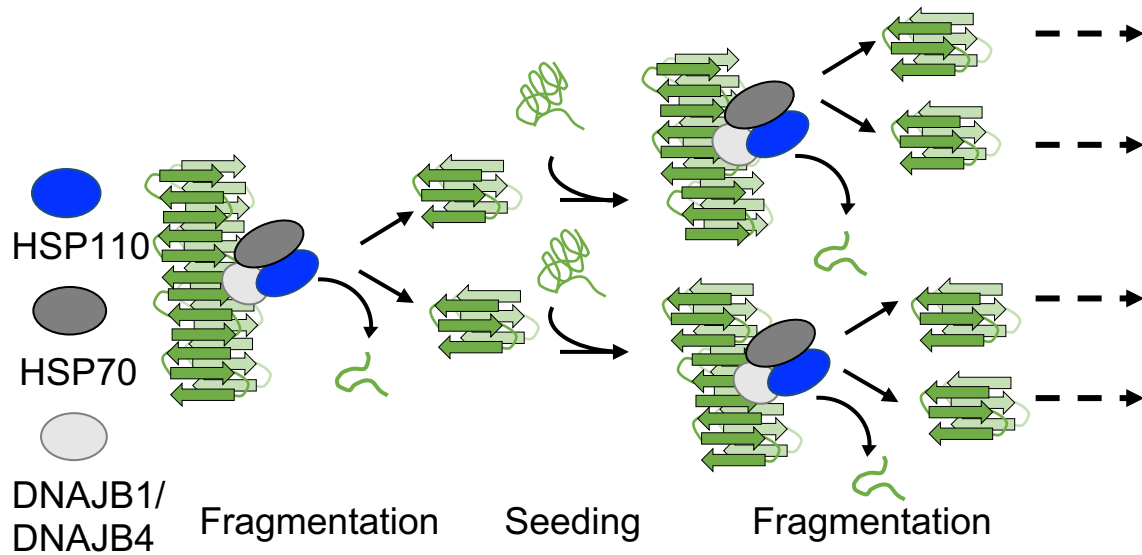
➤ KD of Hsp-110 impairs Hsp70-mediated disaggregation and reduces aggregation, toxicity...



...and spreading of alpha-Syn



# Summary and Outlook



→ **Generation and amplification of toxic species**

## ➤ **Molecular Chaperones: A Double-Edged Sword in Neurodegenerative Diseases**

- Chaperone-mediated amyloid disaggregation might play a role in the progressive spreading of these diseases?
  - chaperone therapy by blocking this activity?
  - specifically targeting DNAJ-amyloid interaction?
  - conformational specificity?