Protein aggregation disorders: from clinic to therapy

Organizers: Ronald Buijsen[1], Laura Donker Kaat[2], Wim Mandemakers[2], Vered Raz[1]

[1] *Department of Human Genetics, Leiden University Medical Center, Leiden*
[2] *Erasmus Medical Center, Rotterdam*

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Location: **Erasmus MC, Rotterdam**

Aberrant protein homeostasis can lead to accumulation and aggregation of proteins in insoluble cellular structures. Protein aggregation is a hallmark feature of many adult neurodegenerative and neuromuscular disorders although the genetic cause and symptoms of these diseases highly varied. Despite varied genetic causes for the protein aggregation disorders, many of these diseases sharing common cellular and molecular mechanisms. Accumulation of proteins and subsequently its aggregation is caused by malfunctioning of protein homeostasis and protein folding machineries. Also aberrant protein homeostasis is a hallmark of aging tissues, in neurodegenerative and neuromuscular disorders the effect is more pronounced and is associated with pathology. Some disorders, such as OPMD, FXTAS and polyglutamine disorders are rare and have a clear genetic component while for more common disorders such as ALS, Alzheimer and Parkinson, there is often no clear genetic cause. Thus, genetic variants of protein aggregation disorders are important in the unravelling of the molecular and pathological processes of more common protein aggregation disorders.
This course will discuss the main molecular mechanisms regulating protein homeostasis and protein folding with a focus a mechanistic foundation in protein aggregation disorders. We will focus on four selected diseases and will discuss genetic, clinic, and current knowledge of disease mechanisms and models for examples. The end point of this course will be development of novel therapeutic strategies to combat protein aggregation in pathological conditions.

Programme

Day 1, November 19th 2026, Erasmus MC Room OWR-45 en 46

Morning session:

08:45-09:15 Registration and coffee

09:15-09:30 Introduction: an overall concept for protein aggregation and pathological conditions, similarities and variations between condition (spectrum of conditions, genetics, causes) and the path to therapeutics.

Session 1: Molecular Mechanism regulating protein accumulation and folding: molecular regulators of protein aggregation.

09:30-10:15 Lecture 1: Autophagy — *Mario Mauthe (UMCG)*

10:15-11:00 Lecture 2: The UPS — *Monique Mulder (LUMC)*

11:00-11:15 coffee and tea break

11:15-12:00 Lecture 3: Chaperones — *t.b.a.*

12:00-12:30 Discussion molecular mechanisms — *all speakers morning session*

12:30-13:30 Lunch break

Afternoon session:

Session 2: Pathology of protein aggregation

13:30-14:15 Lecture 4: Muscle pathology — *t.b.a.*

14:15-15:00 Lecture 5: Cellular mechanisms underlying inclusion pathology in neurodegenerative diseases — *Tim Moors (AmsterdamUMC)*

15:00-15:20 coffee and tea break

Session 3: Protein aggregation in disease

15:20-15:50 Lecture 6: Clinical description of protein aggregation disorders — *Agnita Boon (EMC)*

15:50-16:20 Lecture 7: Protein aggregation in the clinic, FTD as an example — *Laura Donker Kaat (EMC)*

16:20-17:00 Discussion

17:00-18:00 Drinks and meet with the speakers.

Day 2, November 20th 2026, Erasmus MC Room OWR-45 en 46

***Morning session*:**
Session 4: Translational session – disease models and therapy developments
9:00-9:30 Lecture 1: disease modeling of protein aggregation disorders
Wim Mandemakers (EMC)
9:30-10:15 Lecture 2: Dutch ALS centre, clinics, genetics, disease mechanism, therapeutical approaches and clinical trials. *Pavol Zelina (UMCU)*
10:15-10:45 Lecture 3: Therapy development in the lab *t.b.a.*

10:45-11:00 coffee and tea break

11:00-11:45 Lecture 4: Gene therapy as potential therapeutic *Vered Raz (LUMC)*
11:45-12:30 Lecture 5: Small molecules therapy for HD *Sabine Schipper-Krom (AMC)*

12:30-13:30 Lunch break

Afternoon session:
Session 6: Interactive session
13:30-16:00 *An interactive session on aspects you learned during the course*
Ronald Buijsen, Laura Donker Kaat, Wim Mandemakers, Vered Raz
16:00 drinks