



UNIVERSITÀ  
DEGLI STUDI  
DI PADOVA

HORIZON EUROPE  
PROJECTS FUNDED AT THE UNIVERSITY OF PADUA

## **INTEGRATE** - Intramitochondrial seeding and sorting of protein aggregates

Quality control processes maintain mitochondrial health, enabling cellular functions including bioenergetics, metabolism, Ca<sup>2+</sup> signaling, and cell death regulation. Mitochondrial proteases, unfolded protein response, asymmetric fission, vesicle shedding, and mitophagy all contribute to organelle quality. However, the specific triggers for these processes remain unclear. While unfolded protein accumulation appears to be a common event preceding these diverse responses, the mechanism by which it initiates them remains uncertain.

To investigate this question, we developed advanced tools for real-time imaging of protein aggregation in mitochondrial subcompartments. Aggregates in the matrix and intermembrane space induce mitochondrial fission and elicit distinct functional responses based on their location, in a process of early seeding and sorting of protein aggregates.

In the INTEGRATE project, we aim to comprehensively understand the underlying principles and consequences of this process. By combining advanced imaging techniques, omics analysis, biochemistry, functional assays, and unbiased screenings, we will decipher the rules governing aggregate formation, seeding, sorting, cellular fate, and response in various mitochondrial subcompartments.

INTEGRATE seeks to establish the occurrence and downstream responses of this newly discovered early phase of mitochondrial quality control. Clarifying this fundamental mechanism will provide insights into mitochondrial and cell biology, with significant implications for pathological conditions and aging, where mitochondrial quality control is compromised.

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**Coordinator:** Università degli Studi di Padova

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