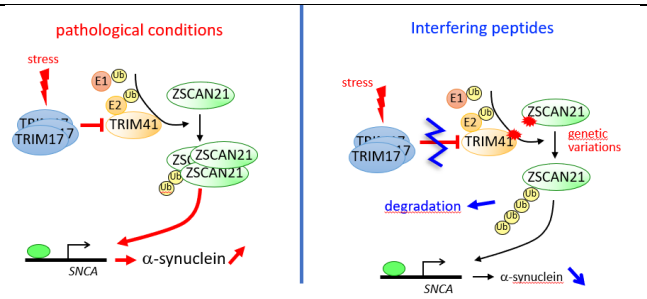
Institut de Génétique Moléculaire de Montpellier
IGMM / CNRS – Université de Montpellier
1919 Route de Mende, 34293 Montpellier Cedex 05

2027 Internship Offer

Master 1: YES – Duration: 2 month **Master 2**: YES – Duration: 6 month

Team, Contact	Thierry Forné lab, Supervisor Irena Lassot: irena.lassot@igmm.cnrs.fr
Title	Modulation of alpha-synuclein expression as a potential therapeutic target in Parkinson's disease
Research Themes and questions	Accumulating data indicate that even a limited increase in wild-type α-synuclein (αsyn) expression can cause both familial and sporadic forms of Parkinson's disease (PD). We have identified a pathway regulating αsyn expression in which TRIM41 mediates the degradation of the transcription factor ZSCAN21 while TRIM17 stabilizes it by inhibiting TRIM41. Silencing ZSCAN21 or TRIM17 prevents both transcriptional induction of αsyn and neurodegeneration in PD models. Furthermore, we identified in familial PD cases variants in ZSCAN21 and TRIM41 genes resulting in ZSCAN21 accumulation and increased αsyn expression. Therefore, our data strongly suggest that this pathway play a crucial role in the transcriptional induction of αsyn that causes PD. Our goal is to modulate this pathway using interfering peptides to enhance ZSCAN21 degradation and restore levels of αsyn that are compatible with neuronal survival in order to halt the progression of the disease.
Methods and experimental approaches	Various experimental approaches *in vitro* and in cells (2 different models of Parkinson's disease) to validate peptide/protein interactions and the inhibitory effects of peptides (recombinant proteins or proteins overexpressed in cells) using co-immunoprecipitation and TSA (thermal shift assay). RTqPCR or digital PCR on total RNA or chromatin-RNA to see the effects of peptides on αsyn expression in cellular models of the disease.
Illustration	
2-3 Publications	- Kozoriz A, et al., *Cell Death Dis*. 2025 May 16;16(1):394. - Basu-Shrivastava M, et al., *Cells* 10: 1235 (2021). - LASSOT I. et al., *Cell reports* 25: 2484-2496.e9. (2018).