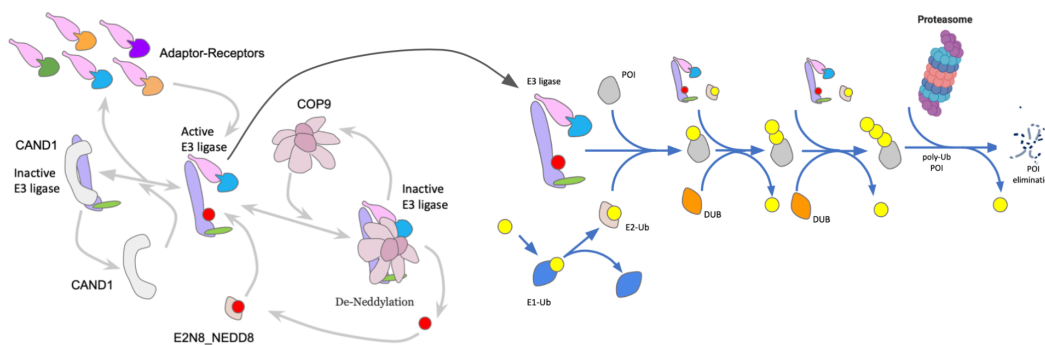


Simulating the ubiquitination system

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In the cell, the degradation of proteins is mediated by a complex pathway which involves the ubiquitin-proteasome system (UPS)¹. This is a core cellular function, where the proteasome recognizes and degrades proteins to maintain the quality of the cellular material and regulates the cell cycle. Malfunction of the UPS pathway is related to several neurodegenerative diseases and cancer². Within the UPS pathway, E3 ligases are macromolecular complexes that catalyze protein ubiquitination, a post-translational modification that labels proteins for proteasomal degradation. Cullin-RING ubiquitin ligases (CRL) are a large superfamily of multicomponent ligases (>600 members). Controlling their function is a promising strategy for therapeutic development³. This project will focus on the development of a platform for integrative kinetic modeling of E3 ligase assembly and function. The Master intern will develop kinetic models as a set of time-ordinary differential equations of the concentration of the molecular species involved in a reaction, develop the software, and produce simulation data that will provide information on the ubiquitination process and the dependency on the kinetic parameters.



Pathway of E3 regulation and ubiquitination of the substrate (protein of interest, POI).

The Master intern should have a keen interest in mathematical modelling, bioinformatics, and programming. She (he) will develop his work in the [DAMM](#) team at the Laboratoire de Biologie et Modélisation de la Cellule (LBMC).

1. Pohl, C. & Dikic, I. Cellular quality control by the ubiquitin-proteasome system and autophagy. *Science* (2019). doi:10.1126/science.aax3769
2. Hwang, J. T., Lee, A. & Kho, C. Ubiquitin and Ubiquitin-like Proteins in Cancer, Neurodegenerative Disorders, and Heart Diseases. *International Journal of Molecular Sciences* (2022). doi:10.3390/ijms23095053
3. Bulatov, E. & Ciulli, A. Targeting Cullin-RING E3 ubiquitin ligases for drug discovery: Structure, assembly and small-molecule modulation. *Biochemical Journal* (2015). doi:10.1042/BJ20141450