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SEMINAIRE

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« Quantification and modulation of in-cell protein folding stability »

Proteins fold and function in the densely crowded and highly heterogeneous cell, which is filled up to a volume of 40% with macromolecules. That under such conditions cells can keep their proteome folded and organized without uncontrollable aggregation is a remarkable aspect of biology. In this talk, I will first discuss how the different cosolutes in the cellular milieu such as ions, crowders and osmolytes govern the protein folding equilibrium. I will thereby present a novel classification scheme of cosolute effects based on their thermodynamic fingerprints. This model is of fundamental importance to understand how the proteome stability is modulated by cellular processes, e.g. to understand how osmolytes or chaperones protect the proteome or how most destabilized proteins aggregate under different cell stresses. I will further present spectroscopic probes that explore the different cosolute effects directly in cells and show that cell stress can significantly modulate the folding equilibrium. Remarkably, protective cellular mechanisms such as the heat shock response or the regulatory volume increase are highly adapted to minimize the impact on the proteome. I will further present novel inhibitors for protein aggregation as a new therapeutic approach for neurodegenerative diseases.

Mardi 12 mars 2019
15h00

Salle de conférence