

03 May
2023

Wednesday
LECTURE

MEET & EAT*

Light lunch provided

11 am - 12 noon

12.15 - 1.15 pm



Protein folding and misfolding on the ribosome

ABSTRACT

At the critical intersection of synthesis and folding, the ribosome is emerging as a hub, guiding the emergence of the polypeptide-chain into the crowded cytoplasm. The ribosome orchestrates elongation rates as well as co-translational binding of folding chaperones, protecting the nascent chain from aggregation. A recent breakthrough from our work revealed that even the final step of folding, the assembly into complexes, is coordinated with translation. However the mechanisms regulating co-translational assembly pathways remain largely obscure. In order to capture and characterize the dynamic pathways of complex assembly, we combined several approaches, including selective ribosome profiling, super resolution imaging, molecular dynamic simulations and proteomics of ribosomes under diverse conditions. Targeting ribosomes overexpressing misfolding-prone proteins we reveal novel quality control factors coordinated with the translation process, discovering a novel pathway for complex subunits that fail to assemble into functional complexes. This provides us, for the first time, direct data on a proteome-wide scale, of factors safeguarding the cellular proteome during synthesis. Using dynamic conformational sampling on several complexes, we identified interface "hot-spot" residues, deriving the exact point during synthesis allowing for a meta-stable complex to form. These predictions directly correlate to the observed onset of co-translational association, demonstrating our ability to predict protein-protein association at the nascent-proteome level. Imaging analysis by smFISH of the translation process in living cells, utilizing super resolution approaches, revealed co-localization of mRNAs encoding for specific complex subunits, in dedicated cytoplasmic foci. Together, our research provides crucial mechanistic insights on protein synthesis, folding and association pathways, opening new horizons for therapy of aberrant protein assemblies, characteristic of numerous conformational diseases.



SPEAKER

Prof Ayala Shiber

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HOSTS:

Department of Infection and Immunity (LIH)
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RESPONSIBLE SCIENTISTS:

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Location:

University of Luxembourg
CAMPUS BELVAL
Maison du Savoir
Room: 2.230
2, avenue de l'Université
L-4365 Esch-sur-Alzette

Webinar via webex:

JOIN

Event number: 2731 088 8277
Event password: MvJYABYR936

Meet & eat:

University of Luxembourg
Campus Belval
Coffee Lounge, 2nd floor, BT1
7, avenue des Hauts-Fourneaux
L-4362 Esch-sur-Alzette