



UNIVERSITÀ
DI TRENTO

Dipartimento di
Biologia Cellulare, Computazionale e Integrata - CIBIO

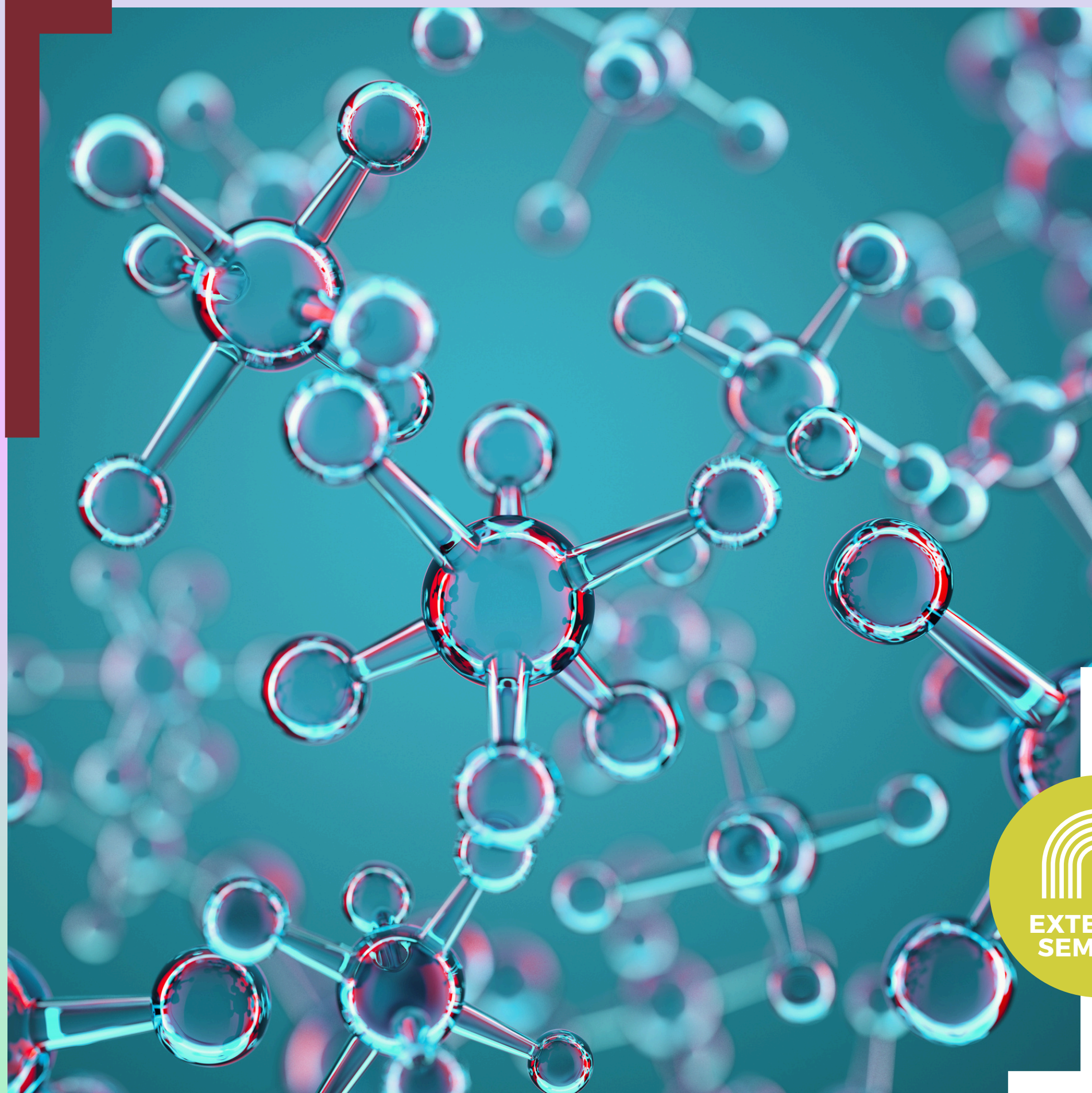
16 JUNE

2:30 P.M.

ROOM A102 - POVO 1

MASSIMO D'AGOSTINO

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II



- ● **ER TRANSLOCATION LANDSCAPE:**
- ● **FROM MOLECULAR MECHANISM**
- ● **TO DRUG DEVELOPMENT**

The translocation of **nascent polypeptides** into the endoplasmic reticulum (ER) occurs through the **Sec61 channel**, guided by **specific signal sequences**. While strong **N-terminal signals** trigger immediate co-translational translocation, weaker or less hydrophobic sequences introduce a **controlled delay**. This delay transiently exposes the polypeptide to the **cytosol**, allowing for pre-translocational modifications (such as phosphorylation) that regulate protein folding, trafficking, and stability. Leveraging the unique nature of these signals, we developed a rapid, sensitive **luciferase-based reporter assay** to screen for **selective Sec61 inhibitors**. These inhibitors can down-modulate specific proteins implicated in human diseases like cancer and inherited disorders, offering promising new avenues for **innovative therapeutic strategies**.