SEMINAR 2025

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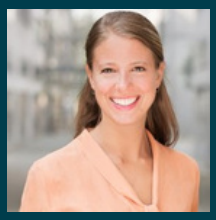
Deciphering protein and lipid interactions by applying correlative approaches



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Host: Aitziber L. Cortajarena

Wednesday, 19th February
12.00 p.m.

CIC biomaGUNE - Seminar Room

The cell membrane, a dynamic protective barrier, is composed of proteins, lipids, and other molecules. Its organization is intricately linked to its function and influenced by interactions with the actin cytoskeleton and extracellular environment at the nano- up to the mesoscale.

To explore the dynamic interplay between lipids and proteins at the nanoscale, I established a correlative approach combining planar photonic nanoantenna arrays, fluorescence correlation spectroscopy (FCS), and atomic force microscopy (AFM). This approach achieved fluorescence enhancements up to 104-105 times and single-molecule detection sensitivity in the micromolar range, enabling the resolution of transient nanoscopic heterogeneities as small as 10 nm on biological membranes. I uncovered a synergistic effect of hyaluronic acid (HA) and cholesterol in reorganizing nanoscale lipid structures. On the living cell membrane I provided direct evidence of transient cholesterol-induced nanodomains (~10 nm) persisting at the sub-30 nm scale.

Building on these findings, I investigated amino acids (AAs) as modulators of weak molecular interactions. Despite their longstanding use as stabilizers in formulations, their mechanisms of action remain elusive. I demonstrated that AAs stabilize weakly interacting proteins, significantly influencing protein self- and cross-interactions even at millimolar concentrations. We proposed and validated experimentally a theoretical framework, attributing this stabilization to weak interactions between AAs and patchy nanoscale colloids, impacting phase behavior, liquid-liquid separation, and binding affinities. I performed quantitative studies using the second osmotic virial coefficient (B22) to reveal the capacity of AAs to stabilize protein self-interactions. For cross-interactions, detectable changes were observed at protein-to-AA stoichiometric ratios as low as 1:1, with binding affinities shifting by an order of magnitude in the presence of 10 mM AAs. Importantly, these modulations occur without altering the secondary structure of proteins.

Currently, I am investigating how AAs influence cross-interactions between immune system proteins that tightly bind, aiming to uncover the molecular drivers underlying these modulations. This research advances our understanding of the molecular principles governing protein-lipid and protein-protein interactions, with broad implications for biomolecular stability and protein function.