INSTITUT PASTEUR

Cell biology and infection

Seminar

"Deciphering the spatiotemporal and mechanical regulation of integrin and actin regulators at the nanoscale"

presented by Grégory GIANNONE

(Interdisciplinary Institute for Neuroscience, UMR 5297 Bordeaux, France)

Monday, March 13th , 2023 at 12 pm

Auditorium François Jacob

Invited by Guillaume DUMENIL

(guillaume.dumenil@pasteur.fr)

Abstract

Super-resolution fluorescence microscopy techniques revolutionized biomolecular imaging in cells by delivering optical images with spatial resolutions below the diffraction limit of light. The direct observation of biomolecules at the single molecule level enables their localization and tracking at the scale of a few tens of nanometers and opens new opportunities to study biological structures at the scale of proteins inside living cells. We are using super-resolution microscopy techniques and single protein tracking to study adhesive and protrusive sub-cellular structures, including integrin-dependent adhesion sites, and the lamellipodium in migrating cells.

The detection of mechanical forces and their conversion into biochemical signals control cell functions during physiological and pathological processes. Mechano-sensing is based on protein deformations, yet the exact molecular mechanisms in cells remain unclear. Using a novel cell stretching device compatible with super-resolution microscopy, we capture the acute mechanical response of individual proteins inside integrin-based focal adhesions. Using this method, we showed that cells respond to external forces by amplifying transiently and locally cytoskeleton displacements triggering protein stretching in mechano-sensitive structures.

Actin filaments generate forces driving membrane movements during trafficking, endocytosis and cell migration. Reciprocally, adaptations of actin networks to mechanical forces regulate their assembly and architecture. Yet, a direct demonstration of forces acting on actin regulators at sites of actin assembly in cells is missing. The lamellipodium is an archetypal membrane protrusion generated by a branched actin network dependent on the Arp2/3 complex, itself activated by the WAVE complex. Using single protein tracking and optical tweezers, we showed that piconewton forces generated by actin filament elongation mechanically regulate WAVE complex dynamics and function in the lamellipodium during cell migration.