

ARCHITECTURE AND MECHANICS OF THE MACROPHAGE PODOSOME

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Abstract: Podosomes are adhesive and mechanosensitive structures that are composed of a core of F-actin surrounded by adhesion complexes. We have recently shown that podosomes are capable of applying protrusive forces onto the extracellular environment, thanks to the development of a method called Protrusion Force Microscopy, which consists in measuring by Atomic Force Microscopy the nanometre deformations produced by macrophages on a compliant Formvar® membrane. We could measure the protrusive force generated at podosomes and show that it oscillates with a constant period and requires combined actomyosin contraction and actin polymerization. We have also shown that protrusion force varies in a synchronous manner for podosome first neighbors, which suggests a short-range interaction, which regulates their mechanical activity. We are now investigating how podosomes are organised at the nanoscale using DONALD, a 3D nanoscopy technique that provides 20 nm isotropic localization precision, and how this organisation regulates protrusion force generation. In particular, we have elucidated the nanoscale architecture of talin, vinculin and paxillin in podosomes formed by human macrophages and demonstrated that these three proteins sustain protrusion force generated at the podosome core.

References:

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