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Structural organization and dynamics of the cytoskeletal network[1]

TATYANA SVITKINA, Department of Biology, University of Pennsylvania, Philadelphia, PA

Actin cytoskeleton is the major player in mechanisms driving multiple forms of cell motility. Actin filaments cooperating with numerous actin-binding proteins are able to form distinct types of higher order structures: networks and bundles, which are designed for carrying out various functions. One of important actin functions is generation of pushing force for protrusion of a leading edge of motile cells. Lamellipodia and filopodia are the two major protrusive organelles utilized by different cells for leading edge protrusion. Even though both are driven by actin polymerization, lamellipodia and filopodia have strikingly different structural design and use different sets of actin-binding proteins. Lamellipodia, which are broad, flat protrusions are filled with a branched network of actin filaments, which propagates through cycles of dendritic nucleation, elongation, capping, and depolymerization of actin filaments. Filopodia, which are thin cellular processes, contain a tight bundle of parallel actin filaments, which elongates at the tip and depolymerizes from the rear. Although basic models for the leading edge protrusion have been formulated, many questions remain about the molecular design of the protrusive machinery and specific roles of individual molecules. Our approach is to analyze molecular architecture of actin cytoskeleton during protrusion and correlate these data with live cell behavior. Recent progress in understanding the molecular mechanisms of actin-based protrusion will be presented.

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