BIOMATERIALS

Forces in Biomolecular Systems SFB 863

Dissection of Spir function: actin nucleation versus motor protein targeting

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Abstract:

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Spir-1, -2 actin nucleators and formin-2 cooperatively initiate actin filaments at vesicle membranes. In mouse metaphase oocytes actin filaments function as tracks for long-range transport of Rab11 vesicles towards the oocyte cortex. The vesicle motility is mediated by the myosin Vb actin motor protein, which is an effector of the Rab11 small G protein. Here we uncover an intricate link between actin nucleation and the engagement of motor proteins. In model membrane systems, vesicle targeting depends on the Spir-2 FYVE-type zinc finger membrane interaction domain and negatively charges lipids. In a cellular context additional protein-protein interactions are required, as both the knock down of Rab11 and treatment with brefeldin A, a Arf small G protein inhibitor, releases Spir proteins from intracellular membranes into the bulk cytoplasm. We detected a direct interaction between Spir-2 and Arf1 but not between Spir-2 and Rab11. Instead we could immunoprecipitate a tripartite complex of Spir-2, myosin Vb and Rab11. Pairwise expression of wild-type and mutant Spir-2 and myosin Vb proteins revealed that each of them can recruit mutants that would not associate with vesicle membranes on their own. In addition, using a bioinformatics approach, we identified a conserved, yet unrecognized sequence in Spir that is crucial for the interaction with the myosin Vb globular tail domain. Thus, the Spir/myosin interaction plays an important role for the assembly of a stable actin nucleator/motor protein complex at vesicle membranes.

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