Linkers at the membrane-cortical actin interface: only linkers?

Julien Pernier[1], Feng-Chin Tsai[1], Remy Kusters[1], Yosuke Senju[2], Hugo Bousquet[3], Jean-François Joanny[1], Pekka Lappalainen[2], Evelyne Coudrier[3], Patricia Bassereau[1]

[1] *Physico-Chimie Curie , Institut CurieParis, France.*
[2] *Institute of Biotechnology, University of Helsinki, Finland.*
[3] *Cell Biology and Cancer, Institut Curie, Paris, France.*

The cortical actin cytoskeleton is a dynamic and polarized network that grows from the plasma membrane. It is dynamically coupled to the plasma membrane by different types of linkers: type 1 myosin motors, BAR-domains proteins with an intrinsically curved shape and ERM (Ezrin-Radixin-Moesin) proteins that play different roles at the membrane-cortex interface. Using in vitro biomimetic assays, we have evidenced that these linkers influence both the cytoskeleton organization and the localization of cytoskeletal forces on the membrane, thus the cell membrane shape. First, we have shown that the non-processive Myosin 1b has a direct effect on actin dynamics and architecture: it depolymerizes actin at the plus-end, which is due to its catch-bond property (i.e. actin-myosin interaction lifetime is increased by 2 orders of magnitude under load) [1] and it also transforms branched actin network in parallel actin bundles (Pernier, in preparation). The I-BAR domain protein IRSp53 that is a curvature sensor (Prevost et al., 2015), spontaneously forms clusters on membranes, which allows local recruitment of actin nucleators and actin polymerization for the initiation of cellular protrusions such as filopodia (Tsai, in preparation). In contrast, ezrin, the most abundant actin-membrane linker, binds to actin in a phosphorylation-dependent manner and is often found enriched in curved cellular protrusions (for instance microvilli, filopodia). Our in vitro experiments evidence that ezrin is not a curvature-sensor protein but is recruited in protrusions through a direct interaction with the curvature-sensor IRSp53, where it reinforces the interaction between actin filaments and the cell membrane.

[1] Pernier, J., Kusters, R., Bousquet, H., Lagny, T., Morchain, A., Joanny, J.-F., Bassereau, P., and Coudrier, E. (2019). A new actin depolymerase: a catch bond Myosin 1 motor. bioRxiv, 375923.
[2] Prevost, C., Zhao, H., Manzi, J., Lemichez, E., Lappalainen, P., Callan-Jones, A., and Bassereau, P. (2015). IRSp53 senses negative membrane curvature and phase separates along membrane tubules. Nat Commun 6, 8529.