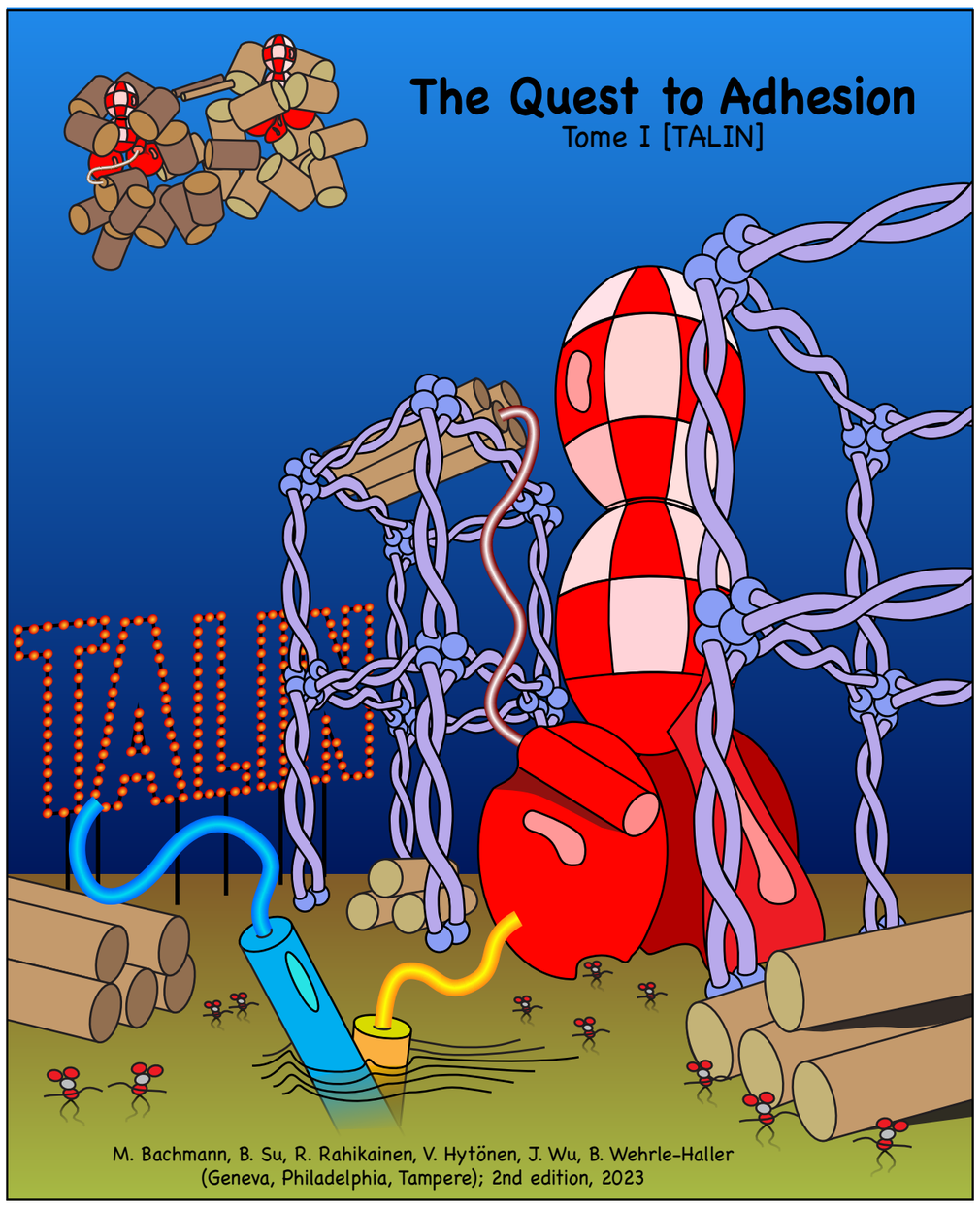
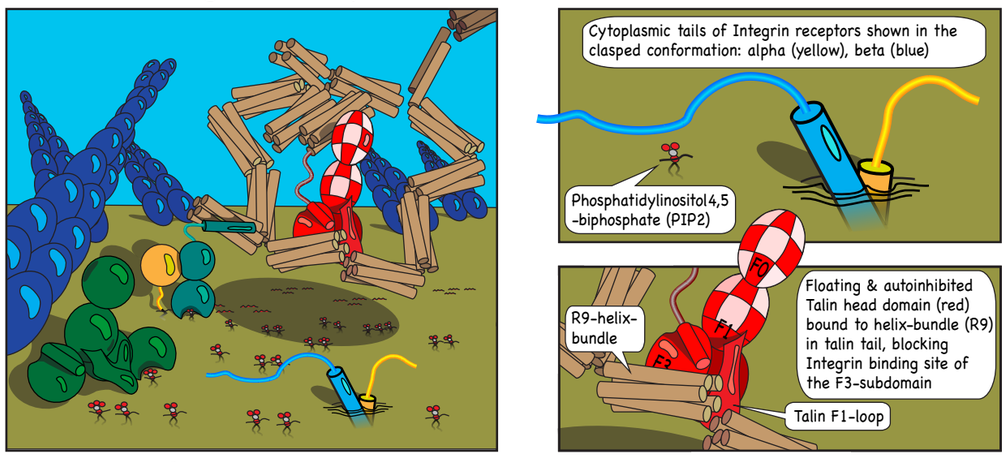
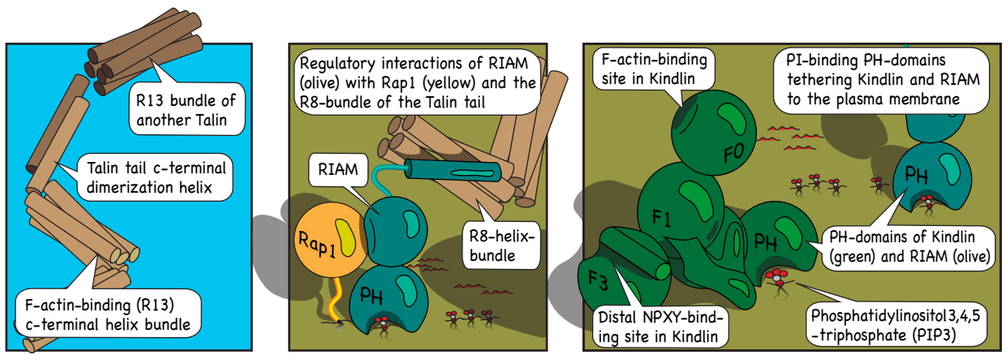


Abstract:

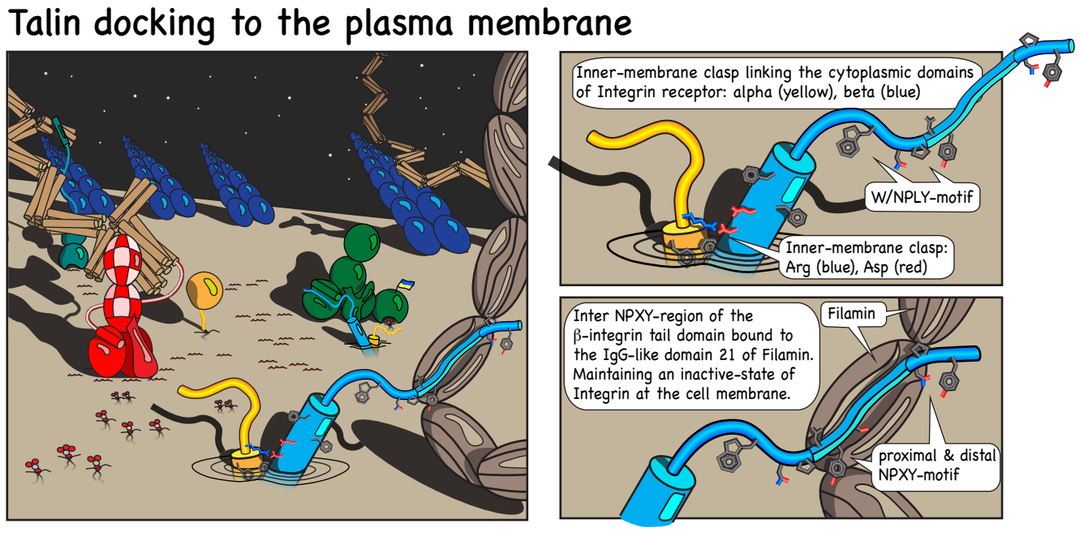
Integrin-dependent cell-matrix adhesions depend on the cytoskeletal adapter protein talin, which dynamically links transmembrane integrin receptors to F-actin. The head domain of talin forms a classic FERM domain, enabling simultaneous interactions with integrins, PIP2 lipids and Rap1. The flexible link to F-actin is provided by helical bundles that offer possibility for regulation, force adaptation and stabilization of integrin-based adhesions. Talin is at the origin of mechanosignaling, occurring at the plasma membrane/cytoskeletal interface, involving the co-adapter kindlin and mediated by the recruitment of the signaling adapter protein paxillin. Here, we visualized the structural and regulatory features of the talin FERM-domain, its association with integrins, Rap1, the involvement of kindlin and RIAM, and the complex force-adapting mechanisms in its flexible tail-domain, consisting of multiple helical bundles. We have opted for a new visual language, illustrating proteins in a cartoon-like style (ligne claire), by emphasizing structural protein changes in a timed animation based on multiple steps, involving: (i) talin membrane mooring, (ii) talin membrane docking, (iii) formation of the talin/integrin/kindlin complex, (iv) integrin activation and force adaptation and the (v) formation of the paxillin-dependent signaling complex.

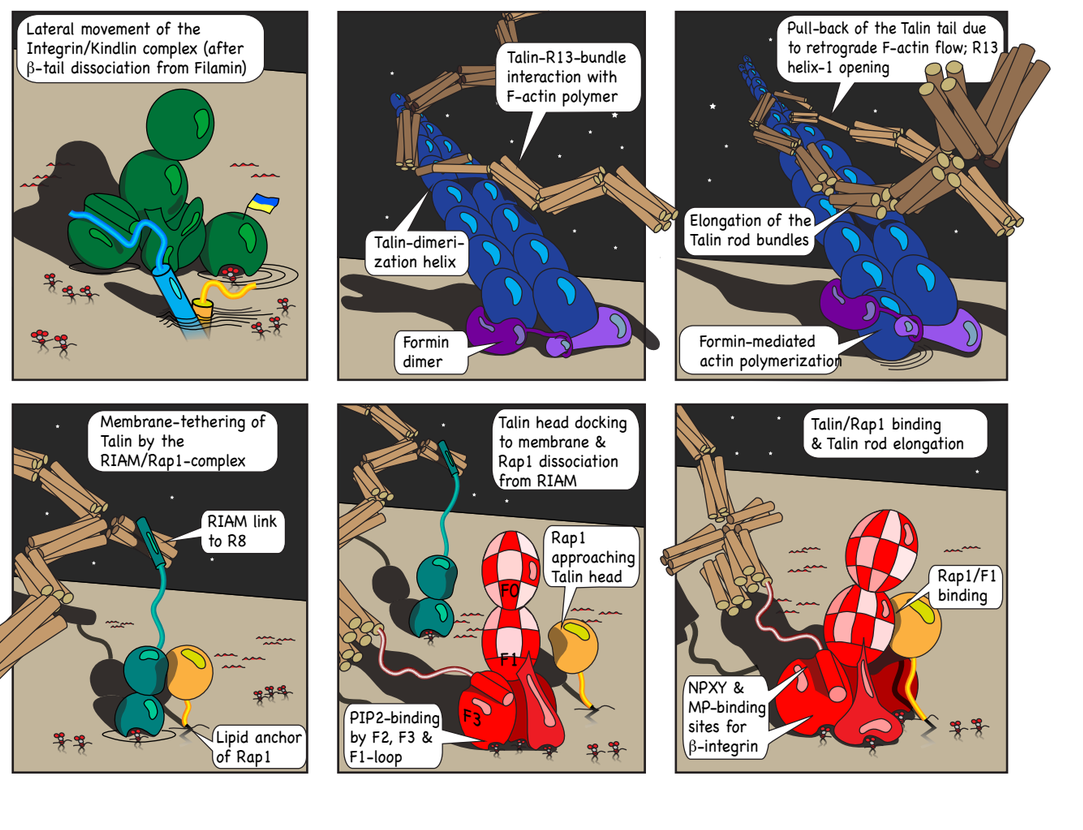
i) Talin mooring to the plasma membrane



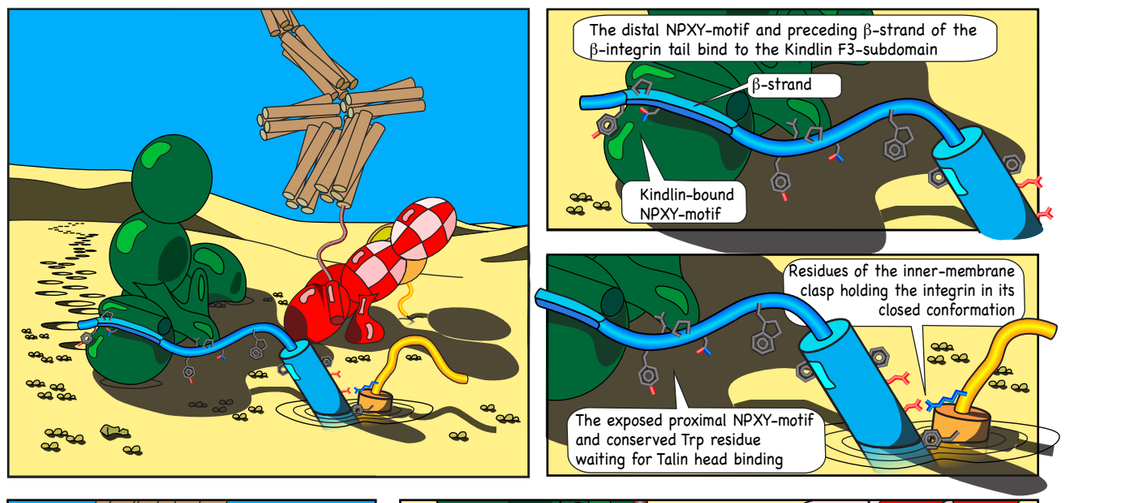


ii) Talin docking to the plasma membrane

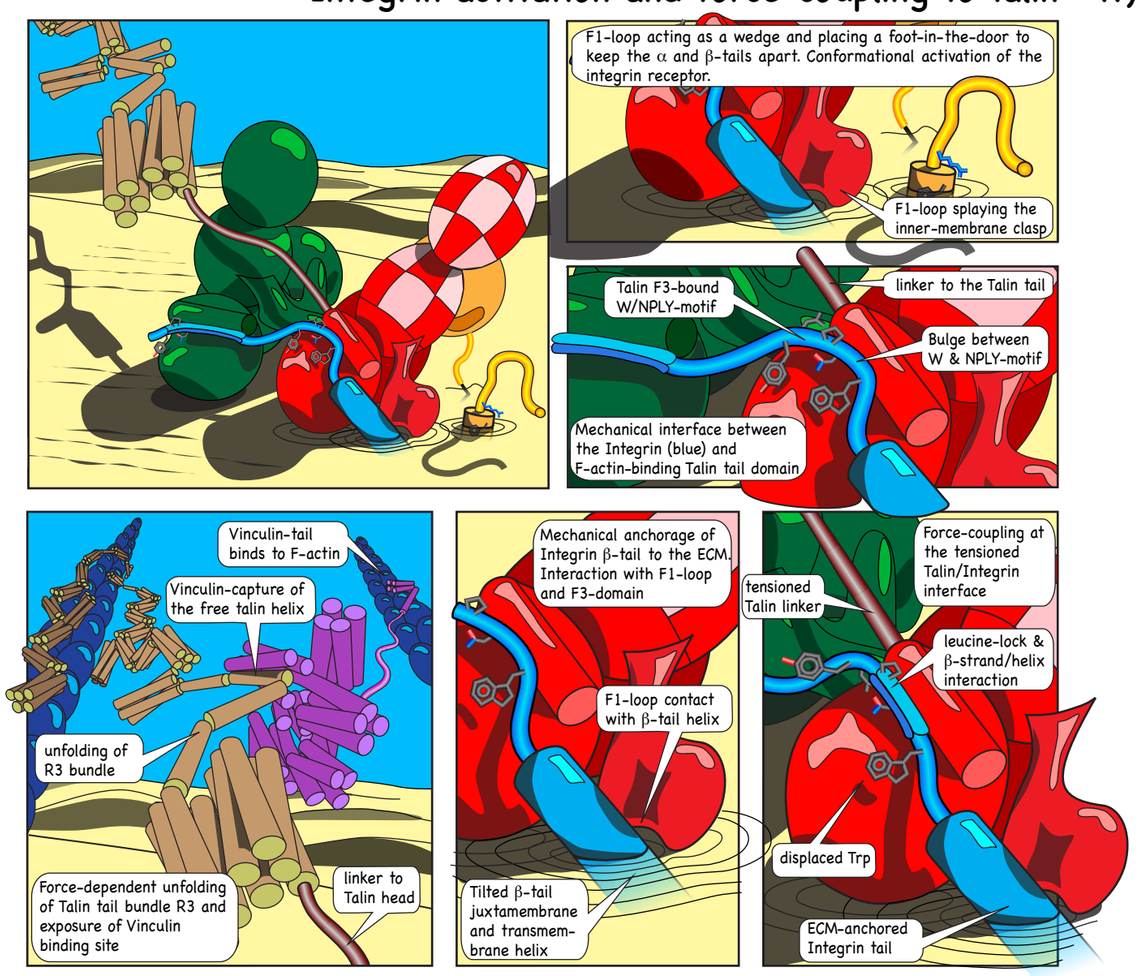




iii) Talin capture by the integrin/kindlin complex



iv) Integrin activation and force-coupling to talin



v) Force-sensing and force-adaptation