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MEMBRANE TRAFFICKING

On track for delivery

Visible by electron microscopy as flask-shaped invaginations of the plasma membrane, caveolae have important functions in signalling, endocytosis and cholesterol transport, but how do they reach their destination in the cell? Wickström *et al.* report in *Developmental Cell* how a serendipitous result led to the elucidation of an adhesion-linked signalling pathway that mediates caveolar trafficking to the cell surface.

Unexpectedly, specifically deleting the gene encoding integrin-linked protein kinase (ILK) from mouse keratinocytes by using the keratin type II cytoskeletal 5 (KRT5) promoter (producing an 'ILK-KRT5' mutant) resulted in the near absence of caveolae, as did deleting β1 integrin. Notably, caveolin 1, the main protein constituent of caveolae, was distributed in the cytoplasm of skin from ILK-KRT5 mutant mice rather than at the basal plasma membrane. ILK-KRT5 keratinocytes had fewer stable caveolae, and caveolin 1-containing vesicles were highly dynamic, whereas re-expressing ILK restored stable plasma membrane caveolae.

Microtubules provide tracks for caveolae to move on, and imaging experiments showed that the movement of caveolae in ILK-KRT5 cells mirrored the highly dynamic lengthening and shortening of microtubules. Microtubules in ILK-KRT5 cells were much less stable than those in control cells, indicating that ILK influences microtubule stability. Inducing microtubule catastrophe in control cells increased membrane dynamics and decreased levels of stable plasma membrane caveolae, indicating that microtubule dynamics regulate caveolar trafficking to the membrane.

Next, the authors found that ILK specifically interacted with Ras GTPase-activating-like protein IQGAP1, an adaptor protein that binds to filamentous actin and the cytoplasmic linker protein CLIP170. The interaction recruited IQGAP1 to the cell cortex, where it is proposed to localize the activity of mDia1 (protein diaphanous homologue 1), an actin-polymerizing formin. mDia1 depletion led to an increase in microtubule and caveolar dynamics, whereas constitutively active mDia1 conferred increased

stability on peripheral microtubules and caused caveolin 1 to redistribute to the cortex.

So, it seems that ILK has an important — and unexpected — function in directing caveolae to the plasma membrane. ILK interacts with IQGAP1, thereby recruiting it to the membrane where, together with mDia1, it can stabilize extending microtubules, allowing them to be tethered to the membrane to deliver their goods.

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ORIGINAL RESEARCH PAPER Wickström, S. A. *et al.* Integrin-linked kinase controls microtubule dynamics required for plasma membrane targeting of caveolae. *Dev. Cell* **19**, 574–588 (2010)