



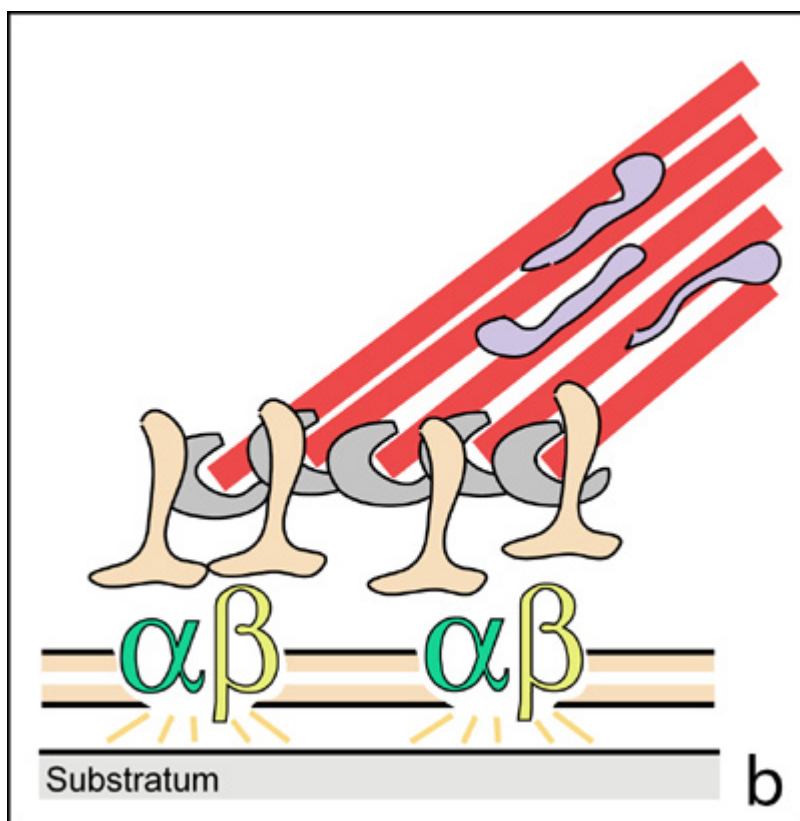
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Substrate Adhesions: The Feet of a Moving Cell

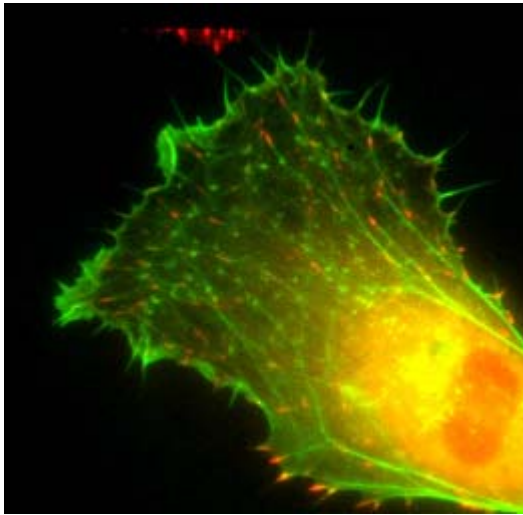
For a cell to move, it must adhere to a substrate and exert traction. Adhesion occurs at specific foci at cytoskeleton on the inside of the cell is linked via transmembrane receptors (integrins) to the extracellular matrix outside. These adhesion sites are composed of complexes of more than 50 different proteins (Zamir and Science 114: 3583-3590, 2001), including structural, signaling and adaptor molecules (Fig 13).



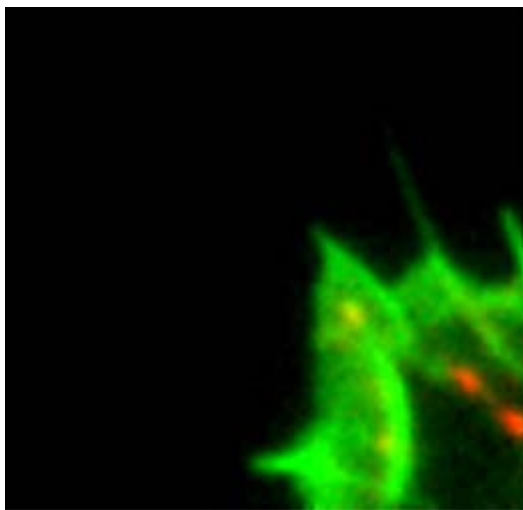
**Figure 13:** Highly simplified schematic illustration of the organisation of a focal adhesion complex. Transmembrane integrins (alpha-beta) are linked to the extracellular matrix ligands on the outside of the cell. Inside the cell, a complex of molecules is linked to actin filaments. At focal adhesions, actin filaments are bundled by actin-binding proteins and contractile proteins. Tension in the bundle, generated by the contractile proteins, is required to maintain the cluster and the integrity of focal adhesions. (Chrzanowska-Wodnicka, 1996)

Adhesion foci can be visualised in living cells by tagging single proteins belonging to the adhesion complex with a fluorescent probe. The adhesion sites are initiated under lamellipodia and filopodia as focal complexes. Focal complexes can either form and dissolve, with a lifetime of around 1-2mins, or can persist and differentiate into focal adhesions (F.A., Fig. 5). Examples of this differentiation from focal complexes to focal adhesions is shown in Figs 14 and 15. Focal complexes and focal adhesions formed at the advancing cell front remain stationary on the substrate.

**Figure 14 :** The formation of substrate adhesions in a migrating goldfish fibroblast. The cell is stained with GFP-actin (green) and microinjected with rhodamine-tagged vinculin (an adhesion protein, red). The protruding cell front is marked with a dashed line.

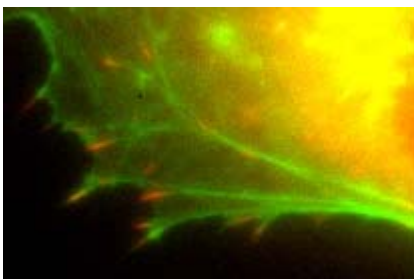


band of actin filaments (the lamellipodium contains radial filament bundles (filopodia) beyond the cell edge. Different types of focal adhesions (red) can be distinguished: small foci (focal adhesions) in lamellipodia and filopodia (focal complexes) behind the lamellipodium, larger foci (focal adhesions) in filopodia. Focal adhesions are also observed at the protruding cell edges (bottom region). Focal adhesions remain stationary, relative to the substrate. Focal adhesions at the retracting edge are produced by Olga Krylyshkina: Nat Rev. Mol. Cell Biol. 2002). (Movie 5)



**Figure 15 :** A detail of the video in the origination of adhesion foci in lamellipodia and filopodia. (Movie 5)

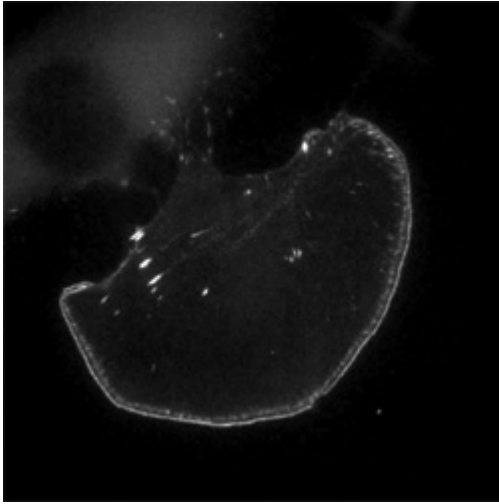
If protrusion of a front ceases, the cell edge retracts to the level of the outermost focal adhesions. Further the sliding and eventual detachment of these adhesion sites. This is the scenario at the rear and flanks (Movie 16).



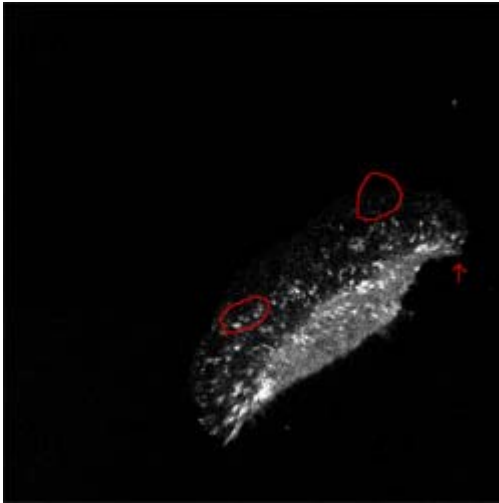
**Figure 16 :** A detail of the retracting region of the cell in sliding focal adhesions (Movie 602Kb)

Different cell types use different adhesion strategies to move. The faster moving cell types show a high degree of complexity as compared to focal adhesions. Examples of alternative adhesion strategies are shown for Dictyostelium cell and for a fish keratocyte in Figs 17 and 18.

**Figure 17 :** Adhesion dynamics at the rapidly migrating



mouse melanoma cell moving on laminin. The cell was GFP-VASP, which is recruited to adhesion foci, as well as of advancing lamellipodia. Focal complexes are formed at the front that turnover within 1-2mins. Very few develop into focal adhesions (see top right at stationary cell edge). (Rottner et al., 1999, 1Mb)



**Figure 18 :** Adhesion dynamics in a migrating fish keratocyte. Focal complexes form under the advancing lamellipodium. Focal adhesions, similar to focal complexes, are formed at the rear. These latter adhesions are however short-lived, since they turnover within 2-3 mins. Video courtesy of Kurt Arndt and Cross, 2000). (Movie 671Kb)



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