Molecular dissection and tuning of actin-dependent protrusion

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Abstract

Cell migration is frequently accompanied by protrusion of thin leaflets of cytoplasm called lamellipodia or of rods termed filopodia. Lamellipodia are built of dense networks of actin filaments and are also called 'ruffles' when lifting up- and backwards during protrusion and retraction.

Lamellipodia formation and turnover are controlled by continuous nucleation and elongation of actin filaments as well as their disassembly, but the precise temporal and spatial features of all these processes are not clear.

In recent years, we have employed photomanipulation techniques such as FRAP or photoactivation to obtain more insight into rate and mode of actin filament turnover in different protrusion types. We have also explored mobility and turnover of various regulators of actin filament assembly/disassembly. Our results allowed conclusions about specific biochemical activities mediated by these regulators in protrusions.

This approach is now extended to exploring the consequences of upregulation of such activities on protrusion efficiency, actin structure organization and dynamics.

We are also continuing to combine these efforts with the inhibition or elimination of specific pathways regulating actin assembly/disassembly in lamellipodia, including for instance the Rac/WAVE/Arp2/3 complex pathway or ADF/cofilin. Examples for these will be discussed.

Collectively, these experiments are aimed at defining the precise biochemical activities operating in space and time during protrusion initiation, maintenance and retraction, and both at the individual filament level or at the larger scale of networks and bundles.