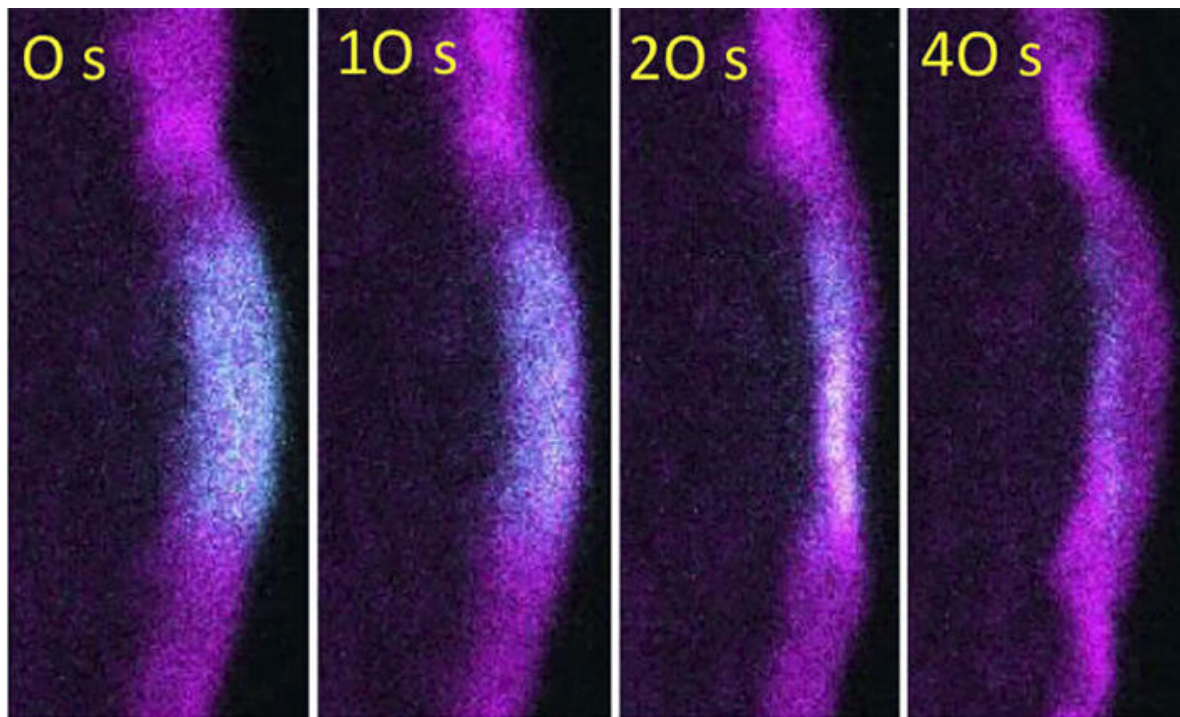


How cells recycle the machinery that drives their motility?

February 9 2021



Time-lapse images of a leading edge of Twf1/Twf2-knockout cell expressing mCherry-LifeAct (magenta) to visualize actin filaments. This cell also expressed photoactivated PA-GFP-actin (cyan), whose decay over time reveals the rate of actin filament disassembly. Credit: Lappalainen Research Group

Research groups at University of Helsinki and Institut Jacques Monod, Paris, discovered a new molecular mechanism that promotes cell

migration. The discovery sheds light on the mechanisms that drive uncontrolled movement of cancer cells, and also revises the 'text book view' of cell migration.

The ability of [cells](#) to move within our bodies is critical in wound healing, as well as for immune cells to patrol in our tissues to hunt bacterial and viral pathogens. On the flip-side, uncontrolled movement of cells is a hallmark of cancer invasion and metastasis.

The machinery that drives cell migration is a complex network of dynamic filaments composed of a [protein actin](#). Actin exists in monomeric form, but like Lego bricks, different types of filamentous structures can be built from actin monomers in cells. Actin filaments are organized in cells in a way that their rapidly elongating plus-ends face the [plasma membrane](#), whereas their minus-ends are oriented away from the plasma membrane. Elongation of [actin filaments](#) at their plus-ends against the plasma membrane generates the force to push the leading edge of cell forward during cell migration. To maintain a sufficient supply of monomeric actin subunits for [filament](#) elongation, actin filaments must be rapidly disassembled in cells, and this is believed to occur at their minus-ends. An important factor that limits actin filament disassembly to their minus-ends is Capping Protein, which binds very tightly to filament plus-ends to block filament elongation and shortening (see related figure).

A new study published in *Nature Cell Biology* reveals that this 'text book view' of cell migration needs to be revised. The research, led by Academy Professor Pekka Lappalainen from HiLIFE Institute of Biotechnology, University of Helsinki, revealed that a conserved actin-binding [protein](#), Twinfilin, efficiently removes Capping Protein from the filament plus-ends ends. This leads to filament depolymerization also from their 'aged' plus-ends, which no longer push the leading edge of cell forward. In the absence of Twinfilin, actin filament recycling is

diminished, filaments push the cell edge forward less efficiently, and [cell migration](#) is slower.

"Our results suggest that Twinfilin and Capping Protein make together a 'molecular clock', which ensures that the 'productive' actin filaments pushing the plasma membrane have a sufficient supply of actin monomers, whereas the 'aged' actin filaments that no longer push the plasma membrane are disassembled," says Lappalainen.

"This study highlights the need of several proteins with different functions to act in synergistic manner to maintain the normal morphology and functions of actin networks in cells," continues Dr. Markku Hakala who is the main author of this study.

Despite extensive studies, the precise mechanisms by which actin monomers are recycled in cells has remained elusive. The new study adds an important piece in this puzzle by revealing how Capping Protein is removed from actin filament plus-ends to enable their rapid disassembly. These findings also create a basis for further studies to understand how irregularities in [actin](#) disassembly machinery cause severe diseases and developmental disorders.

"Uncontrolled expression of Twinfilin is linked to many diseases, such as breast cancer invasion and lymphoma progression. Our work, therefore, also sheds light on the molecular mechanisms that drive uncontrolled movement of cancer cells," concludes Lappalainen.

More information: Markku Hakala et al, Twinfilin uncaps filament barbed ends to promote turnover of lamellipodial actin networks, *Nature Cell Biology* (2021). [DOI: 10.1038/s41556-020-00629-y](https://doi.org/10.1038/s41556-020-00629-y)

Provided by University of Helsinki

Citation: How cells recycle the machinery that drives their motility? (2021, February 9) retrieved 23 June 2024 from <https://phys.org/news/2021-02-cells-recycle-machinery-motility.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.