The Arp2/3 inhibitory protein Arpin controls directional persistence of cell migration by inducing idling phases

Roman Gorelik and Alexis Gautreau*

CNRS UPR3082,
Laboratoire d'Enzymologie et Biochimie Structurales,
Avenue de la terrasse
91190 Gif-sur-Yvette, France

* Corresponding author:
alexis.gautreau@lebs.cnrs-gif.fr

Keywords: *cell migration, branched actin network, lamellipodium, feedback loop, Rac*

Abstract

We recently reported the identification of Arpin, a protein that inhibits the Arp2/3 complex at the lamellipodial edge. Arpin is activated by the small GTPase Rac, suggesting that Arpin contributes to intrinsic instability of lamellipodia, consistent with the frequent observation that lamellipodia protrude and retract. We previously reported in three different model systems of cell migration, namely the human cell line MDA-MB-231, the amoeba *Dictyostelium discoideum* and primary fish keratocytes that Arpin decreases the two major parameters of cell migration, cell speed and directional persistence, thus making Arpin an efficient inhibitor of cell migration. To understand how Arpin can control both migration parameters, we undertook a biphasic analysis, which distinguishes active phases from idling phases, where cell speed drops below a threshold. This speed threshold, which fits all 3 systems of migration, despite their different migration characteristics, is calculated through a simple formula depending on average speed and the first derivative of mean squared displacement. We found that cells change direction during idling phases, highlighting that directional persistence is intrinsically connected to cell speed. Importantly, Arpin induces idling phases in all 3 systems of cell migration. This role of Arpin thus explains and unifies the simultaneous control of both parameters of cell migration, cell speed and directional persistence. The decrease of the duration of the active migration phase by Arpin is consistent with a signalling circuit, in which Arpin antagonizes the Rac-dependent positive feedback loop that sustains actin polymerization and active protrusion at the cell front.