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A calcium dependent de-adhesion mechanism regulates the direction and rate of cell migration: A mathematical model

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Abstract

Cell migration has long been studied by a variety of techniques and many proteins have been implicated in its regulation. Integrins, key proteins that link the cell to the extracellular matrix, are central to adhesion complexes whose turnover defines the rate of cell locomotion. The formation and disassembly of these adhesions is regulated by both intracellular and extracellular factors. In this study we have focused on the Ca2+-dependent protein network (module) that disassembles the adhesion complexes. We have developed a mathematical model that includes the Ca2+-dependent enzymes μ-calpain and phospholipase C (PLC) as well as IP3 receptors and stretch activated Ca2+ channels, all of which have been reported to regulate migration. The model also considers the spatial effects of Ca2+ propagation into lamella. Our model predicts differential activation of calpain at the leading and trailing edges of the cell. Since disassembly of integrin adhesive contacts is proportional to the degree of calpain activation, this leads to cell migration in a preferred direction. We show how the dynamics of Ca2+ spiking affects calpain activation and thus changes the disassembly rate of adhesions. The spiking is controlled by PLC activity and currents through stretch-activated Ca2+ channels. Our model thus combines the effects of various molecular factors and leads to a consistent explanation of the regulation of the rate and direction of cell migration.

Keywords

μ-calpain regulation, Adhesion turnover, Calcium, Cell detachment, Cell migration, Cell polarization, Mathematical modelling