BMC Bioinformatics



Oral presentation



# The Important Role of Calcium in Regulation of Adhesion Disassembly and Cell Migration: Mathematical Modelling

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*from* BioSysBio: Bioinformatics and Systems Biology Conference
Edinburgh, UK, 14–15 July 2005

Published: 21 September 2005

*BMC Bioinformatics* 2005, **6**(Suppl 3):S15

Cell migration is crucial for many functions in metozoan organisms, such as embryonic development, wound repair, cancer invasion and immunity. Migration involves actin-nucleation based membrane protrusion, new focal adhesion formation and focal adhesion disassembly. Calpain is a Ca2+-dependent enzyme that localizes to focal adhesion, cleaves a large number of adhesion proteins and is believed to be involved in disassembly of focal adhesions. An elegant experiment by Franco et al. 2004 showed that calpain cleavage of talin is a rate limiting process in adhesion disassembly. One of the two calpain isoforms, μ-calpain, is activated by micromolar Ca2+. It has been demonstrated that calcium fluxes are capable of activating μ-calpain, which is required for cell motility of keratinocytes. Stretch-activated Ca2+ channels are major regulators of cell migration and are believed to be involved in Ca2+-dependent μ-calpain activation. However, the mechanism of the Ca2+-dependent μ-calpain activation remains poorly characterized. Here we develop a model for Ca2+ dynamics and Ca2+-dependent μ-calpain activation. The model includes a number of Ca2+-dependent proteins: Ca2+-dependent PLCδ (and also Ca2+ independent PLC), IP3 channels on the ER membrane, the calcium pumps, and stretch activated Ca2+ channels. We show that stretch activated channels may work as a switch, turning Ca2+ oscillations on or off. Increases in calcium activate μ-calpain, causing μ-calpain activity impulses. The amplitude, frequency and duration of the impulses have been studied as a function of the system's components, in particular as a function of Ca2+-dependent and independent PLC activities. The implications for Ca2+-dependent μ-calpain activity in adhesion turnover are discussed.