ABSTRACT

Nucleus is the largest cellular organelle in animal cells. Due to its bulky nature and the stiffness of nuclear lamina the nucleus constitutes the substantial problem for migrating cells where nucleus has to move. The actomyosin generated forces and LINC (Linker of Nucleoskeleton and Cytoskeleton) complex, that is composed of SUN and nesprin proteins, play key role in nuclear movement. LINC complex mechanically couples nuclear lamina to the cytoskeleton and allows the forces exerted by the cytoskeleton to move the nucleus. Perinuclear actin fibers, also termed actin cap, mechanically link focal adhesions with nucleus and they may generate forces that position the nucleus in a way that is optimal for cellular movement. However, molecular mechanism of how perinuclear actin fibers and LINC complex orchestrate the nuclear movement and functional significance of this process remain poorly understood.

The specific aim was to determine the mechanisms by which perinuclear actin fibers are formed and how are these mechanisms employed to facilitate cell migration. The role of LPA-RhoA signaling axis and LINC complex in the formation of perinuclear actin fibers was also examined.

It was confirmed that LPA is essencial stimulus during actin cap formation. On the other hand, FAK kinase was found necessary for actin cap disassembly during cell polarization. Our results also indicate that actin cap increases directionality of cell migration without affecting cell velocity. In contrast with previous assumtion, it was found that actin binding domain of nesprin-2 does not significantly influence connection of perinuclear actin fibres to the LINC complex and formation of actin cap.

key words: LINC, perinuclear actin, actomyosin contractility, cell migration, LPA, Rho, FAK