UKE Paper of the Month April 2018

Lymphocyte-specific protein 1 regulates mechanosensory oscillation of podosomes and actin isoform-based actomyosin symmetry breaking

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ABSTRACT: Subcellular fine-tuning of the actomyosin cytoskeleton is a prerequisite for polarized cell migration. We identify LSP (lymphocyte-specific protein) 1 as a critical regulator of actomyosin contractility in primary macrophages. LSP1 regulates adhesion and migration, including the parameters cell area and speed, and also podosome turnover, oscillation and protrusive force. LSP1 recruits myosin IIA and its regulators, including myosin light chain kinase and calmodulin, and competes with supervillin, a myosin hyperactivator, for myosin regulators, and for actin isoforms, notably beta-actin. Actin isoforms are anisotropically distributed in myosin IIA-expressing macrophages, and contribute to the differential recruitment of LSP1 and supervillin, thus enabling an actomyosin symmetry break, analogous to the situation in cells expressing two myosin II isoforms. Collectively, these results show that the cellular pattern of actin isoforms builds the basis for the differential distribution of two actomyosin machineries with distinct properties, leading to the establishment of discrete zones of actomyosin contractility.

STATEMENT: *Our data identify LSP1 as a novel central regulator in actomyosin-driven migration of primary human macrophages. They also have high translational potential, as they give a detailed molecular explanation for the known LSP1-based defects in immune cell migration in diseases such as rheumatoid arthritis and Neutrophil Actin Dysfunction (NAD) and thus open up ways for exploring novel therapeutic approaches.*

BACKGROUND: This work was performed at the Institute for Medical Microbiology, Virology and Hygiene in the group of Stefan Linder, who holds a professorship at UKE since 2009. It was part of the PhD thesis of Pasquale Cervero. The authors have strong research interests in the field of cytoskeletal regulation and intracellular trafficking, with a special focus on macrophage biology and pathophysiology.