Filamin in cell mechanics and mechanotransduction

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Abstract

Living cells are subjected to internal and external mechanical forces that can elicit biochemical signals in response to the applied forces (mechanotransduction). Mechanotransduction plays a crucial role in tissue repair and regeneration by controlling cell migration, growth, and differentiation. It is responsible for exercise-induced bone mass maintenance, muscular dystrophies, and hypertension-induced vascular and cardiac hypertrophy. Despite its importance, little is known about the underlying mechanisms of mechanotransduction. We have recently identified filamin (FLNA), an actin filament cross-linking protein, as a mechanotransduction mediator of mechanical input to biochemical output. The seminar will discuss about 1) how FLNA cross-links actin filaments, 2) the role of FLNA in cell mechanics, 3) the atomic structure of a FLNA-partner complex, 4) mechanical properties of FLNA molecule and FLNA- actin networks, 5) how mechanical forces regulate FLNA-partner interactions, and 6) visualization of conformational changes of the FLNA-mechanosensing domain in live cells.

Faculty Academic Appointments

04/95-03/01	Associate Professor	Environmental Bioremediation	Tohoku University
08/06-01/08	Instructor	Medicine	Harvard Medical School
02/08-present	Assistant Professor	Medicine	Harvard Medical School

5 Selected publications

Nakamura F, Song M, Hartwig JH, Stossel TP. Documentation and localization of force-mediated filamin A domain perturbations in moving cells. *Nat Commun*. 2014;5:4656 PMID 25120197, PMC 4139033

Gomez-Mouton C, Fischer T, Peregil RM, Jimenez-Baranda S, Stossel TP, **Nakamura F**, Manes S. Filamin A interaction with the CXCR4 third intracellular loop regulates endocytosis and signaling of WT and WHIM-like receptors. *Blood*. 2014 PMID 25355818

Sun C, Forster C, **Nakamura F**, Glogauer M. Filamin-A regulates neutrophil uropod retraction through RhoA during chemotaxis. *PLoS One*. 2013;8(10):e79009 PMID 24205360, PMC 3808352

Xu T, Lannon H, Wolf S, **Nakamura F**, Brujic J. Domain-domain interactions in filamin A (16-23) impose a hierarchy of unfolding forces. *Biophys J*. 2013;104(9):2022-30 PMID 23663845, PMC 3647155

*Ehrlicher AJ, ***Nakamura F**, Hartwig JH, Weitz DA, Stossel TP. Mechanical strain in actin networks regulates FilGAP and integrin binding to filamin A. *Nature*. 2011 PMID 21926999 (*co-first authorship)

Editorial Activities

2010-present	Associate Editorial Board	The American Journal of Translational Research

Ad hoc Reviewer

Structure
EMBO Reports
Journal of Applied Physiology
Journal of the National Cancer Institute
Blood
Proteins
Molecular and Cellular Biology
PNAS
Carcinogenesis
Journal of Biological Chemistry
Pigment Cell & Melanoma Research PLoS ONE

Human Mutation
Journal of Pediatric Genetics
Journal of Cell Science
Neuron
Molecular Biology of the Cell
Cell and Tissue Research
BBA
Human Molecular Genetics
Neuron
Nature Communications
Cardiovascular Research
Scientific Reports
Circulation Research
Cell Proliferation