Cell Communication and Signaling BioMed Central

Meeting abstract

Open Access

Crosslinking of microtubules and actin filaments by S100A8/S100A9

M Wolf*[1], C Riethmüller[2], B Petersen[1], H Oberleithner[2], J Roth[1] and T Vogl[1]

Address: [1]University of Münster, Institute of Immunology, Münster, Germany and [2]University of Münster, Institute of Physiology II, Münster, Germany

* Corresponding author

from 12th Joint Meeting of the Signal Transduction Society (STS). Signal Transduction: Receptors, Mediators and Genes
Weimar, Germany. 29–31 October 2008

Published: 26 February 2009

Cell Communication and Signaling 2009, **7**(Suppl 1):A103 doi:10.1186/1478-811X-7-S1-A103

This abstract is available from: http://www.biosignaling.com/content/7/S1/A103

Microtubules (MT) and actin filaments of phagocytes exhibit highly dynamic properties. The underlying molecular mechanisms are not entirely known. Their exceptional dynamic cytoskeleton is the prerequisite of many phagocyte related functions like exocytosis, phagocytosis, and in particular migration. Cell dynamic/migration is a highly complex process strictly regulated by numerous signaling cascades often initiated by changes in cytosolic calcium concentrations. Therefore, calcium-binding proteins are key elements in signal transduction. The major calcium-binding molecules expressed in granulocytes and monocytes are myeloid-related protein 8 (MRP8 [S100A8]) and MRP14 (S100A9), two members of the S100 protein family. MRP8 and MRP14 form heterodimers in the absence and tetrameric complexes composed of two heterodimers in the presence of calcium.

We demonstrate that MRP8/MRP14 tetramers promote MT polymerization as well as MT bundling; moreover, the complex crosslinks MTs to F-Actin in a strictly calcium dependent manner. HEK293 cells transfected with MRP8/MRP14 contain significantly more polymerized tubulin in comparison to mock-transfected cells. These results are in line with reduced level of polymerized tubulin in phagocytes isolated from MRP14 -/- mice. Furthermore, phagocytes of MRP14 knockout mice show altered migration rates compared to wildtype cells. In addition to calcium-induced activation the MRP8/MRP14 complex can be specifically phosphorylated by p38 mitogen-activated protein kinase (MAPK), which abrogates MT/F-Actin crosslinking. Thus MRP8/MRP14 integrates signals of at least two independent signaling pathways. Our results provide evidence, that the MRP8/MRP14 complex fulfils a pivotal role in remodeling cytoskeletal structures necessary for migration of leukocytes.