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Fibulin-1 is an adhesion-modulating component of the hematopoietic stem cell niche

Schreiber TD¹, Hergeth SP^{1,4}, Aicher WK², Essl M¹, Sasaki T^{3,5}, Klein G¹

¹ Section for Transplantation Immunology and Immunoematology, Center for Medical Research, University Medical Clinic, Tübingen, Germany

² Center for Medical Research, Department of Orthopedic Surgery, University of Tübingen, Germany

³ Max-Planck-Institute for Biochemistry, Martinsried, Germany

⁴ present address: Spemann Laboratories, Max Planck Institute of Immunobiology, Freiburg, Germany

⁵ present address: Department of Biochemistry, Oregon Health and Science University, Portland, USA

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In the bone marrow stem cell niche, osteoblasts lining the endosteum are of major importance in supporting hematopoietic stem cell maintenance and controlling self-renewal. Here, we report on the expression of the fibulins, highly conserved calcium-binding glycoproteins that are components of the extracellular matrix of human osteoblasts. We also provide insights into their functional relevance in the stem cell niche. All six members of the fibulin family were detected by RT-PCR. The expression of fibulin-1 and -2 was verified by Western blot analysis. Two-color immunofluorescence staining revealed a co-localization of both fibulins with fibronectin in an extracellular meshwork. Fibulin-2, but not fibulin-1, appeared to be instantly degraded by active metalloproteases present in osteoblast cultures. Fibulin-2 was shown to be a substrate for MMP-2, which was constitutively secreted by primary osteoblasts, as assessed by gelatin zymography. Whereas fibulin-2 exhibited cell binding properties towards the hematopoietic progenitor cell line KG1a, fibulin-1 was capable of modulating adhesion to fibronectin, resulting in the disturbance of fibronectin-induced cell signaling pathways, as analyzed

with an anti-phosphotyrosine antibody. Thus, fibulins seem to be important components of the extracellular matrix of osteoblasts, which are likely to influence the adhesive properties of the stem cell niche towards hematopoietic stem cells.

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