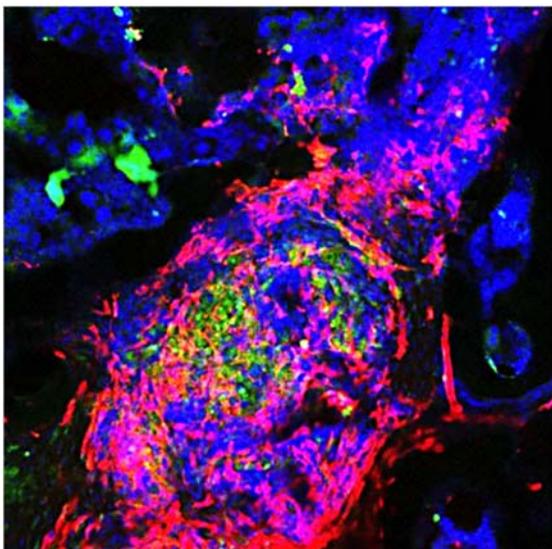


Important cellular and molecular mechanisms of bone marrow fibrosis in hematopoietic malignancies discovered

Aachen, 28.04.2017 – Bone marrow (BM) fibrosis is a fatal disorder in which normal bone marrow tissue and blood-forming cells are gradually replaced with thick coarse fibers and scar-like tissue. Over time, this leads to failure of the body to produce blood cells and ultimately to death. The specific mechanisms that cause BM fibrosis are not understood, in particular, as the cells driving fibrosis have remained obscure. The laboratories of Rafael Kramann (Division of Nephrology and Clinical Immunology, Uniklinik RWTH Aachen) and Rebekka Schneider (Division of Hematology and Oncology, Uniklinik RWTH Aachen and Department of Hematology, Erasmus Medical School, Rotterdam) and their collaboration partners have now revealed the cellular origin of BM fibrosis.

In their work published today in Cell Stem Cell ([http://www.cell.com/action/showMethods?pii=S1934-5909\(17\)30079-6](http://www.cell.com/action/showMethods?pii=S1934-5909(17)30079-6)), they demonstrate that Gli1 marks a subset of bone marrow stromal cells that turn into scar forming myofibroblasts upon exposure to malignant hematopoietic stem cells. Importantly, the authors show that genetic ablation or pharmacologic targeting of these cells by Gli protein inhibition abolishes bone marrow scar formation (fibrosis) and rescues bone marrow failure (anemia) in mice. Furthermore, the authors demonstrate that the same pathway is active in human disease where Gli1 expression correlates with disease severity. Therefore, Gli inhibition might be a promising novel therapeutic strategy. This work has important implications for both better understanding of the disease, for improved diagnostics and for improved treatments, as bone marrow fibrosis is regarded as an incurable disease.



Gli1+ mesenchymal stromal cells (red) expand during myelofibrosis and become scar forming myofibroblasts that drive bone marrow fibrosis and replace hematopoietic cells.

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About Uniklinik RWTH Aachen

Uniklinik RWTH Aachen is a supramaximal healthcare provider that combines patient-oriented medicine and nursing with world-class teaching and research. The University Hospital covers the entire spectrum of medicine with 34 specialist clinics, 25 institutes and five interdisciplinary units. Outstandingly qualified teams of doctors, nurses and scientists commit themselves competently to the patient's health. Bundling healthcare, research and teaching in one central building provides optimum conditions for intensive interdisciplinary dialogue and a dense clinical and scientific network. Around 7,000 personnel provide patient-oriented medical care and nursing in compliance with recognised quality standards. The University Hospital has 1,400 beds and treats approximately 48,000 inpatients and 183,000 outpatients every year.