The Team:
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Study Programme Experimental Medicine Student: B. Meier
Additional Members of Thesis Advisory Committees: M. Berneburg (Tübingen), C. Buske (Ulm), D. Kletsas (Athens), C. Mauch (Cologne), C. Niessen (Cologne), R. Nischt (Cologne), K.L. Rudolph (Jena/Ulm), A. Wells (Pittsburgh), S. Wells (Cincinnati), T. Wirth (Ulm), L. Wiesmüller (Ulm), G. Van Zant (Lexington)

Department of Dermatology and Allergic Diseases

Work Group:
Aging: Mechanisms and Novel Preventive Strategies

Head: Karin Scharffetter-Kochanek

Life expectancy has risen in developed societies and the mystery of aging has still not been resolved. The prevalence of infectious, autoimmune, endocrine and mental diseases and of connective tissue degeneration has sharply increased. We are testing the hypothesis whether oxidative stress and/or DNA damage pathways are of general relevance to the intrinsic and extrinsic aging of the connective tissue and life span. The connective tissue-specific SOD2 deficient mouse shows a complex aging phenotype. We are interested in the role of free radicals and its impact on signaling pathways involved in the organization of the extracellular matrix, organ maintenance, metabolic homeostasis and renewal capacities of stem cells (Karmveer Singh). The DNA damage response pathway (DDR) resulting in cellular senescence is addressed in dermal fibroblasts (Florentina Ferchiu). Stromal cells influence the tumorigenesis of skin tumors. The role of senescent fibroblasts in tumor progression is investigated on the cellular and organismic levels (Vida Farsam). The complex cellular interactions in aging are addressed in a systems biology approach with specific focus on NFkB (Patrick Meyer). The nucleolus is studied as stress sensor of DDR and related signaling pathways (Robin Assfalg) that possibly also affect ribosomal biogenesis (Sylvia Koch). The regenerative and repair effect of mesenchymal stem cells (MSC) and their mediators is analyzed in acute wound healing in mice (Yu Qi). Molecular and cellular mechanisms of wound repair by MSC in mouse models of impaired regeneration are analyzed (Andrea Kügler).
Work Group: Hematopoiesis and Hematopoietic Stem Cells

Head: Hartmut Geiger

Hematopoiesis is the process by which mature blood cells are formed from hematopoietic stem cells (HSC). Research in our laboratory is centered on stem cell aging, leukemia and DNA damage responses. In mice and humans there is a successive decline in stem cell function from adulthood to old age. This decline has been associated with perturbed tissue homeostasis and impaired injury repair in aged individuals. HSCs from aged animals are impaired by their inability to self-renew, to contribute efficiently to hematopoiesis and to differentiate. Our hypothesis is that distinct molecular and cellular pathways contribute to stem cell aging. Our data supports the view that the elevated activity of small RhoGTPases found in hematopoietic cells in aged animals results in altered adhesion to stroma cells. We were able to demonstrate that aged stem cells are more active inside the bone marrow niche in vivo, which most likely results in less stable stem cell stroma interactions. Altered adhesion to the niche/stroma could be one underlying cause for phenotypes associated with aged HSCs. Altered DNA damage response pathways in aged HSCs might be critical for increased incidence of age-associated disease. We are developing molecular tools to determine DNA damage responses in HSCs (Bettina Überle). Aging in stem cells might contribute to an increase in leukemia with age. We are interested in determining whether the age of the stem cell niche/stroma influences leukemia development (Novella Guidi).