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Laboratory of Transgenic Models of Diseases & Transgenic Unit

Cell-extracellular matrix interactions, proteases and their inhibitors, transgenesis & embryo manipulations

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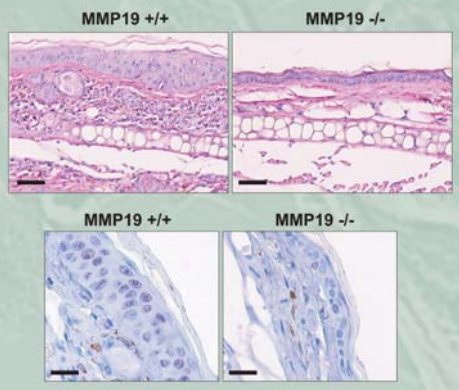
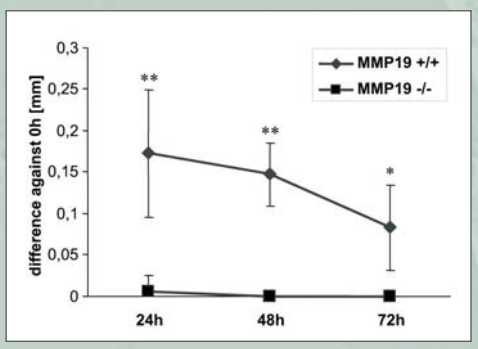
Research topics

Interactions of cells with their surroundings, i.e. the extracellular matrix, is essential for development and functional organization of specialized tissues and organs. The cell-matrix interactions control cell differentiation, survival, migration, and activation via cell surface receptors and adhesion molecules. Especially adhesion molecules sense changes in the composition of extracellular matrix that is affected by proteases and their inhibitors. Balance between these two molecule classes determines if tissues and organ architecture are to be built up or disrupted. Thus, this balance is pivotal for tissue homeostasis and its disturbance leads to development of various pathologies such as cancer, chronic inflammation, or fibrosis.

Our current research focuses on investigating the role of selected metallo- and serine proteases, and their inhibitors in two biological compartments: liver and epidermis/epithelium. Regulated expression of proteases in the epidermis and many epithelia is crucial not only to maintain the body and organ barriers, but also for regulation of local inflammatory reactions. To further the understanding of development and progression of liver fibrosis and inflammation processes, our research in this area analyses the effects and consequences of metalloproteinase-mediated turnover of extracellular matrix and the release of regulatory molecules from the cellular surfaces, a process that is mediated by shedding proteases.

In addition to the research activities we have set up, in the middle of 2008, a Transgenic Unit that offers embryo manipulating services including DNA pronuclear microinjections, sperm freezing and archiving, *in vitro* fertilization (IVF), embryo isolations, rederivation of mouse lines/strains, vasectomy, etc.





MMP19-deficient mice show impaired contact hypersensitivity model (CHS) reaction: influx of inflammatory cells (upper panel), keratinocyte proliferation (middle panel), and ear swelling (lower panel).

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Selected recent papers

Beck IM, Rückert R, Brandt K, Mueller MS, Sadowski T, Brauer R, Schirmacher P, Mentlein R, Sedlacek R. MMP19 is essential for T cell development and T cell-mediated cutaneous immune responses. **PLoS ONE.** 2008;3:e2343.

Generation of transgenic mice. DNA microinjection into pronucleus of murine zygote: left, zygote before insertion of microcapillary; middle, zygote during microinjection; right, two-cell stage embryos developing from the manipulated eggs.