LABORATORY OF

INTEGRATIVE BIOLOGY

Mechanobiology, cytoskeleton, cytolinkers, cell junctions, simple epithelia

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In the past five years, our main research interests have been:

1. cytoskeleton-dependent regulation of cell-cell contacts in simple epithelia;
2. regulation of cell-matrix adhesions; and
3. cytoskeleton and adhesion-mediated signalling in epithelial-mesenchymal transition, cell migration and invasiveness.

We mainly focus on cytoskeletal linker proteins, in particular plectin, and we study the functional consequences of cytoskeletal organization in cell/tissue mechanics and mechanotransduction, i.e., conversion of physical cues into intracellular mechanosignalling pathways. To fulfil our aims in the complexity of biological systems, we use a combination of in vitro (primary cells and CRISPR/Cas9-targeted cell lines) and in vivo (transgenic models) approaches. Besides conventional molecular biology techniques, we also employ methods that enable us to measure and apply physiologically relevant forces and deformations, such as traction force and atomic force microscopy, magnetic tweezer rheology, cell stretching, and FRET-based tension sensors.

As the Laboratory of Integrative Biology team was established as part of BIOCEV (in January 2015), our long-term interest is also defined by BIOCEV Project 1.1.4.: „Mouse models for studying of physiology and pathophysiology of digestive epithelia" (the Functional Genomics Programme).

This aim has the following core project objectives:

1. identification of genes with unique and essential functions in simple epithelia;
2. generation of mouse models with targeted selected genes; and
3. phenotypic characterization of generated mouse models addressing gene functions in healthy and diseased simple epithelia.

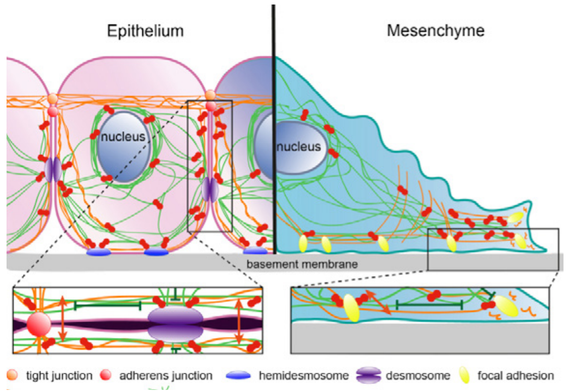

Figure 1. Schematic overview of plectin localization and plectin-mediated crosslinking/anchoring in epithelial (left) and mesenchymal (right) cells.

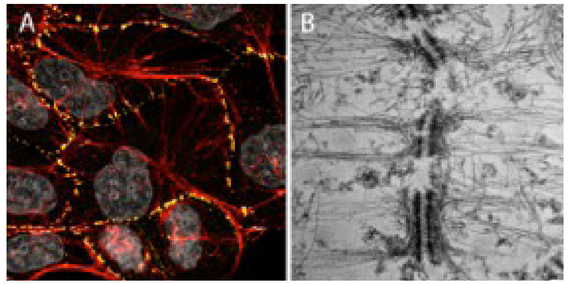

Figure 2. (A) Defective organization of keratin filaments (red) and desmosomes (yellow) in epithelial cells with an inactivated gene encoding the binding protein plectin. (B) Non-functioning desmosomes and keratin filaments imaged by transmission electron microscopy.

Selected publications:

1. Prechova M, Adamova Z, Schweizer AL, Maninova M, Bauer A, Kah D, Meier-Menches SM, Wiche G, Fabry B, Gregor M*: Plectin-mediated cytoskeletal crosstalk controls cell tension and cohesion in epithelial sheets. J Cell Biol 2022 221(3):e202105146.
2. Gerckens M, Schorpp K, Pelizza F, Wögrath M, Reichau K, Ma H, Dworsky AM, Sengupta A, Stoleriu MG, Heinzelmann K, Merl-Pham J, Irmler M, Alsafadi HN, Trenkenschuh E, Sarnova L, Jirouskova M, Frieß W, Hauck SM, Beckers J, Kneidinger N, Behr J, Hilgendorff A, Hadian K, Lindner M, Königshoff M, Eickelberg O, Gregor M, Plettenburg O, Yildirim AÖ, Burgstaller G*: Phenotypic drug screening in a human fibrosis model identified a novel class of antifibrotic therapeutics. Sci Adv 2021 7(52):eabb3673.
3. Krausova A, Buresova P, Sarnova L, Oyman-Eyrilmez G, Skarda J, Wohl P, Bajer P, Sticova E, Bartonova L, Pacha J, Koubkova G, Prochazka J, Spörrer M, Dürrbeck Ch, Stehlikova Z, Vit M, Ziolkowska N, Sedlacek R, Jirak D, Kverka M, Wiche G, Fabry B, Korinek V, Gregor M*: Plectin Ensures Intestinal Epithelial Integrity and Protects Colon Against Colitis. Mucosal Immunol 2021 14:691.
4. Strouhalova K, Přechová M, Gandalovičová A, Brábek J, Gregor M* , Rosel D*: Vimentin Intermediate Filaments as Potential Target for Cancer Treatment. Cancers. 2020 12(1). pii: E184.