LABORATORY OF

INTEGRATIVE BIOLOGY

Cytoskeleton, cytolinker proteins, cell junctions, simple epithelia, mechanobiology

Martin Gregor

BIOCEV

more information

e-mail

In recent 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. Beside 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, and FRET-based tension sensors . Our findings provided a novel perspective on the exclusivity of actomyosin-mediated contractility for integrin activation and provided the basis for a more in-depth investigation of the role of intermediate filaments in mechanosignalling.

Our long-term interest includes mouse models for studying the physiology and pathophysiology of digestive epithelia. We strive to 1) identify genes with unique and essential functions in simple epithelia; 2) generate mouse models with targeted selected genes; and 3) characterize phenotypes of the generated mouse models, addressing gene functions in healthy and diseased simple epithelia. For example, we generated a mouse model recapitulating the symptoms of *Epidermolysis bullosa* (*EB*) in the liver. Analysis of this model showed that *EB*-associated genes play a crucial role in the liver adaptation to cholestasis. Mutated mice failed to rearrange bile ducts in experimental cholestasis, and bile retention caused significant liver damage (Jirouskova et al., *J. Hepatol.*, 2018). This study highlights the risks in patients with *EB* in combination with bile formation and excretion defects. Our research also has a profound effect on understanding liver fibrosis, inflammatory bowel diseases, and carcinogenesis.

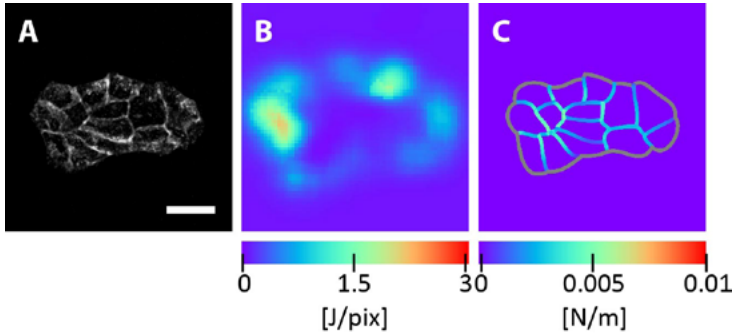

Figure 1. 2D traction force microscopy in cell colonies. **(A)** Colony of MDCK cells labelled with tdTomato-Farnesyl. **(B,C)** Distributions of contractile energy (B) and line tension at cell-cell borders (C) shown as pseudo-colour images. Bar, 30 μm.

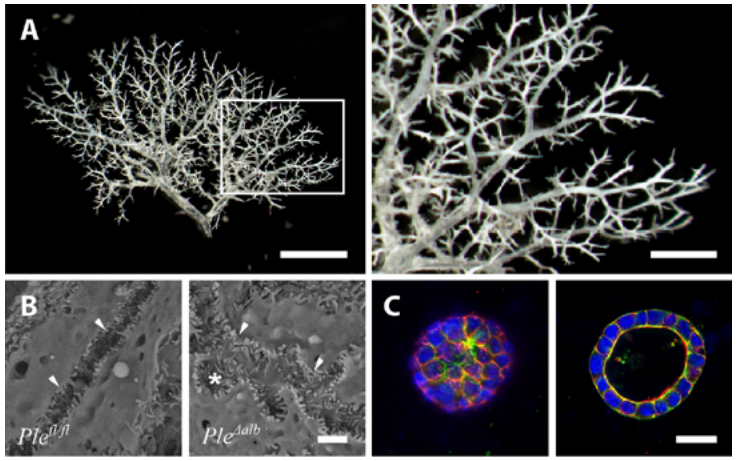

Figure 2. Visualization of biliary tree architecture. **(A)** Acrylic resin cast of biliary tree in the liver lobe of adult mice. Bar, 3 mm. **(B)** Scanning electron images of bile canaliculi in wild-type (*Ple*$^{fl/fl}$; left) and liver-specific plectin knockout (*Ple*$^{•alb}$; right) mouse. Arrowheads, bile canaliculi; asterisk, blind loop in *Ple*$^{•alb}$ canaliculi only. Bar, 1 μm. **(C)** 3D spheroid grown from biliary epithelial cells and immunolabelled using antibodies to pan-keratin (green) and plectin (red). Nuclei stained with DAPI (blue). Bar, 10 μm.

Selected publications:

1. Jirouskova M, Nepomucka K, Oyman-Eyrilmez G, Kalendova A, Havelkova H, Sarnova L, Chalupsky K, Schuster B, Benada O, Miksatkova P, Kuchar M, Fabian O, Sedlacek R, Wiche G, Gregor M* (2018) Plectin controls biliary tree architecture and stability in cholestasis. *J Hepatol*, **68**:1006-1017.
2. Taylor SRA, Malone J, Zhang Y, Prechova M, Kaczmarek LK* (2019) Phactr1 regulates Slack (KCNT1) channels via protein phosphatase 1 (PP1). *FASEB J*, **34**:1591-1601. https://doi.org/10.1096/fj.201902366R
3. Korelova K, Jirouskova M, Sarnova L, Gregor M* (2019) Isolation and 3D collagen sandwich culture of primary mouse hepatocytes to study the role of cytoskeleton in bile canalicular formation in vitro. *J Vis Exp*, **154**. doi: 10.3791/60507.

In the picture: 1. Přechová Magdalena | 2. Krausová (Kalendová) Alžběta | 3. Maninová Miloslava | 4. Gregor Martin | 5. Sarnová Lenka | 6. Adamová Zuzana | 7. Burešová Petra