Histochem Cell Biol (2010) 133:1–40
DOI 10.1007/s00418-009-0665-2

REVIEW

Extending the knowledge in histochemistry and cell biology

Wolfgang-Moritz Heupel · Detlev Drenckhahn

Accepted: 17 November 2009 / Published online: 28 November 2009

Abstract Central to modern *Histochemistry and Cell Biology* stands the need for visualization of cellular and molecular processes. In the past several years, a variety of techniques has been achieved bridging traditional light microscopy, fluorescence microscopy and electron microscopy with powerful software-based post-processing and computer modeling. Researchers now have various tools available to investigate problems of interest from bird's- up to worm's-eye of view, focusing on tissues, cells, proteins or finally single molecules. Applications of new approaches in combination with well-established traditional techniques of mRNA, DNA or protein analysis have led to enlightening and prudent studies which have paved the way toward a better understanding of not only physiological but also pathological processes in the field of cell biology. This review is intended to summarize articles standing for the progress made in "histo-biochemical" techniques and their manifold applications.

Keywords Cell biology · Histochemistry · Microscopy

Advances in ultrastructural, subcellular and cellular visualization of single molecules, cells and tissues

Histochemistry and Cell Biology's half-century anniversary had been celebrated with a series of excellent expert reviews covering both essential cell biological and methodical issues and microscopic techniques (Asan and Drenckhahn 2008; Roth et al. 2008a). State of art cell biological research in the twenty-first century greatly benefits from innovative methodical and technical improvements, which were developed and refined in the last 30 years of the past century.

W.-M. Heupel (✉) · D. Drenckhahn (✉)
Institute of Anatomy and Cell Biology,
University of Würzburg, Koellikerstr. 6,
97070 Würzburg, Germany
e-mail: heupel@uni-wuerzburg.de

Electron microscopy

A large number of reviews and articles focused on advances in electron microscopy (EM). Frotscher et al. (2007) summarized current efforts in biological sample fixation under non-dehydrating conditions. These methods, which include high-pressure freezing of fresh unfixed tissues, are able to preserve the original ultrastructure of the tissue, which is convincingly demonstrated for neuronal synapses and their remodeling under synaptic activity. The researchers did not forget to compare this precise and static view with methods for real-time monitoring of living synapses by fluorescent labeling. Conservation of native ultrastructure for EM was also the topic of three other recent articles. Pierson et al. (2009) (as presented in the Robert Feulgen Lecture 2009) and Studer et al. (2008) focused on imaging macromolecular complexes in their native environment. This can be achieved by combining ultrastructure-preserving techniques like cryo-conservation, or for thicker specimen, cryo-EM of vitreous sections (CEMOVIS), with electron tomography, which is able to reproduce the native three-dimensional ultrastructure. A final step in deciphering molecular complexes at atomic resolution is the fitting of already resolved X-ray or NMR structures into these tomographic images. Using these approaches, fascinating insights into molecular structures of desmosomes have been achieved, resolving these adhesive cell contacts down to interacting cell adhesion molecules of the desmocadherin family (Al-Amoudi et al. 2007; He et al. 2003). In another study, strategies for complementation of cryo-electron

tomography with genetical or pharmacological manipulations and comparative light microscopy (LM) are summarized (Lucic et al. 2008). That way, the impressive images of these innovative EM-based techniques can be also investigated from a functional perspective. In that context, a promising way to detect genetically labeled proteins is the use of the 3,3′-diamino-benzidine (DAB) photoconversion (Meiblitzer-Ruppitsch et al. 2008). Fluorescent signals emanating from a molecule of interest for example can be converted into electron dense DAB-deposits for investigations in EM studies. This is vividly demonstrated for three fluorophores, including green fluorescent protein-variants EGFP and EYFP and boron-dipyrromethene (BODIPY), fused to different molecules, including proteins and lipids. BODIPY-labeled analogs of sphingolipids and cholesterol are often used to study cholesterol and sphingolipids-enriched domains (Marks et al. 2008).

Labeling proteins of interests has been achieved by immuno-EM using gold particles coupled to specific antibodies or protein A long ago (Roth 1996). Mayhew and Lucocq (2008a, b) recently have improved quantitative immuno-EM images for comparing labeling distributions between different compartments and conditions. They further extended the method of estimating (relative) labeling densities to compartments containing both surface-occupying (membranes) or volume-occupying (organelles) antigens.

Two recent studies investigated and further extended long-established EM techniques. Osmium tetroxide is commonly used as a stain in EM and LM. Belazi et al. (2009) now set out to explore binding of osmium tetroxide to specific lipids by using time-of-flight secondary ion mass spectrometry (ToF-SIMS) of mouse adipose tissue. The authors corroborated the view that osmium tetroxide binds to unsaturated lipids, mainly C18. In contrast, ionic abundance and signals at sites of phospholipids and proteins but not near fatty acids are diminished after osmium tetroxide treatment. These novel findings of binding specificity of this commonly used microscopic stain should be taken into account when interpreting images contrasted with osmium tetroxide.

Stradalova et al. (2008) presented a novel protocol for using high-pressure freezing and LR White embedding of mammalian cells. Compared to chemically fixed cells, ultrastructural conservation was improved, but more importantly, immunolabelled densities were found to be significantly increased, demonstrating this technique as an alternative to embedding in Lowicryl resins.

Light microscopy

Ingenious improvements in the field of LM too have been achieved. To extend the limits of traditional LM, researchers combine it with biophysical techniques like atomic force microscopy (AFM) (Doak et al. 2008; Taatjes et al. 2008b), laser microdissection (Emmert-Buck et al. 1996), EM (Giepmans 2008), powerful nanoparticles for contrast enhancement (Debbage and Jaschke 2008), software-based image reconstruction techniques (Stemmer et al. 2008) or even fluorescence in situ hybridization (FISH) (Mingle et al. 2009). In an outstanding review article, Verveer and Bastiaens (2008) gave an excellent schematic overview of state-of-the-art fluorescent microscopical techniques, shedding light into the "F"-keywords, including FRAP (fluorescence recovery after photobleaching), FRET (fluorescence resonance energy transfer), FLIM (fluorescence lifetime imaging microscopy), FCS (fluorescence correlation spectroscopy), TIRF (total internal reflection microscopy) or SFTM (single fluorophore tracking microscopy). Doak et al. (2008) lately introduced an interesting combination of AFM and confocal laser scanning microscopy (AFM–CLSM). The AFM technique has the unique feature to explore surface topologies even of hydrated and unfixed native structures. In combination with CLSM and fluorescent markers, topological features can be correlated with molecular information. By using this technique, ultra-structural ridges on the apical surface of prostate epithelial cells were attributed to punctuate moesin clusters. The authors therefore conclude a direct visualization of moesin linkages between transmembrane proteins and the cytoskeleton.

In a fascinating overview, Lenne described his recent approaches investigating cell-surface dynamics and mechanics (Lenne 2009; Lenne et al. 2008). By using FCS together with nanometric apertures, the resolution limit of molecular diffusion signals was enhanced and signals intensified. By this technique, insights into the association of Drosophila E-cadherin with two different pools of actin filaments and the corresponding acto-myosin network were obtained (Cavey et al. 2008). The author convincingly demonstrated that methodical improvement (e.g. microfabricated nanoapertures) can not only greatly improve already established techniques (e.g. FCS) but also lead the pave for future technologies such as single molecule DNA sequencing (Eid et al. 2009; Lenne et al. 2008).

A novel LM technique has been developed by Mingle et al. (2009). The authors described the methodical details for a technically improved sequentially but combined FRET and FISH technique. In this paper not only a detailed methodical background on this approach was given but also an application was shown to visualize RhoA activation (via a FRET biosensor) and Arp2 mRNA localization in fibroblasts in response to lysophosphatidic acid treatment. This led to an increased and mutually exclusive localization of active RhoA and Arp2 mRNA. Their findings indicate that this method can be adopted for the detection of other FRET-based biosensors and DNA/RNA probes in the same cell.

Raman spectroscopy, e.g. Raman scattering light measurements, has long been used to analyze the chemical compositions of a specimen without the need of labeling. Harada et al. (2009) extended the use of Raman spectroscopy for studying intracellular dynamics by combining it with slit-scanning confocal microscopy. Thereby, the temporal resolution was dramatically increased, allowing detailed investigations on subcellular distributions of proteins without artificial labeling. This is of course limited to special molecules, but its use is demonstrated by tracking the pharmaceutical topoisomerase I inhibitor CPT-11 and its metabolite SN-38 in living cancer cells proving its usefulness for pharmacokinetic studies of anticancer drugs in living cells.

Several studies have been published improving LM labeling techniques. Takechi et al. (2008) presented a method to double-label proteins of interest using polyclonal antibodies of the same species. This at the first glance unfeasible approach is achieved by using a very low dilution of the first primary antibody labeling the first protein of interest, which is only detectable following a biotin-avidin-based amplification. The second protein of interest was assessed via standard secondary antibody detection. As an example, colocalization of enterocytic apolipoprotein B with the Golgi apparatus was demonstrated. The authors proposed this technique to be a quick and cheap method of double-staining when primary antibodies of different species are unavailable. Indeed, based on this technique the authors further demonstrated that in APP/PS1 amyloid transgenic mice, there is a significant colocalization of apolipoprotein B with cerebral amyloid plaques (Takechi et al. 2009).

Blaschitz et al. (2008) investigated the feasibility of using cryo-compatible antibodies in hepes-glutamic acid buffer-mediated organic solvent protection effect (HOPE)-fixated and paraffin-embedded sections, because this kind of fixation showed to induce only low denaturation of proteins and consequently should extend possibilities for immuno-labeling approaches. In differently fixed placenta tissue, cryo-compatible antibodies targeting HLA-G and different leukocyte differentiation antigens were tested yielding good immuno-signals on cryo- and HOPE-fixed but not formalin-fixed paraffin sections.

In his overview, Mandell (2008) critically reviewed immunohistochemical identification of protein phosphorylation using phosphorylation state-specific antibodies (PSSAs). After a historic introduction, the author directed the readers' attention to the unfulfilled expectations of PSSAs. Many studies indeed failed to demonstrate added value of PSSAs over general antibody immunohistochemistry (IHC). Clearly, detailed validation of antibodies in different tissue fixations and preparations has to be done before allowing solid interpretation of phosphosignals by immunohistochemical experiments.

Another study investigated the immunohistological detection of the glycolipid Gb(3) in the mouse kidney and nervous system (Kolling et al. 2008). As an important caveat for all immunohistological studies, the authors found that tissue variations in fixation and processing steps strongly affected the antigenic structure resulting in partially unspecific recognition of Gb(3). For example, Gb(3) localization to endothelial cells in the tissues analyzed was demonstrated to be a fixation artifact.

Camillo Golgi's development of "the black reaction" provided Santiago Ramón y Cajal with a histological silver staining method enabling him to formulate the neuron theory. Orlowski and Bjarkam (2009) recently provided an autometallographic enhancement of the Golgi-Cox staining to gain high resolution visualizations of dendrites and spines. The authors summarized their method to be cheaper and more flexible, compared to other enhancement procedures, and provided detailed methodical explanations together with fascinating images. Their method should deliver enlightening insights into dendrite branching and spine densities.

In LM, experimental pitfalls are not only essentially based on the methodical production of images but can also lie in the storage of the digital files, a fact that is becoming more and more important in times of digital image analysis. A recent work described variations in nuclear roundness in images saved with the JPEG compression algorithm in the context of automated processing of nuclear quantification (Lopez et al. 2009), which extended the authors' prior work (Lopez et al. 2008). Nuclear roundness was significantly affected by image compression and linear correlation factors to correct the discrepancy in the roundness estimate were developed, which, according to the authors, can be easily incorporated in different systems of digital image analysis.

Cellular in vivo imaging

Tracking individual cells in living organisms opens possibilities to directly investigate specific cellular interactions and pathogenic processes. For this, efficient but gentle marking of the cells of interest is essential. In their recent work, Schormann et al. (2008) compared labeling of exogenous human tumor cells with the lipid dye CM-DiI or red fluorescent nanoparticles Qdot655 for the injection and tracking in mice. Furthermore, the authors analyzed if fluorescent signals in unprocessed paraffin sections represent the transplanted cells by using human or mouse ISH probes. Whereas most CM-DiI-marked cells were identified as human cells, some were detected by the mouse probes, probably indicating phagocytosis of the transplanted cells. CM-DiI-positive structures in paraffin sections remained fluorescent also after ISH, but Qdot655-positive structures

faded during further staining procedures. The authors conclude that fluorescent marking of cells prior injections is an efficient method investigating cell behaviors such as migration or invasion in living organisms.

In this context, in vivo assessment of cellular half-life in tissues would be a challenging extension. By analyzing loss of 5-bromo-2′-deoxyuridine (BrdU)-labeled cells over time after withdrawal of long-term BrdU labeling allowed the authors of a recent paper to histologically measure cellular half-life in tissues in vivo (Erben et al. 2008). Subcutaneous pellets slowly releasing BrdU were incorporated into rats for 1 or 3 weeks. After normalizing cellular half-life following withdrawal of BrdU by a nonlinear regression analysis, the authors successfully validated their technique determining a half-life of 2.4 days for crypt cells or of 2.2 weeks for cardiac endothelial cells. As the method could be used in combination with other labeling methods as well, it could be an interesting extension to the tracing method of Schormann et al. (2008).

A morpho-functional protocol for investigating microvascular processing in a living organ was demonstrated recently (Solder et al. 2009). For this sake, vessels of the human placental cotyledon were tagged with a fluorescent tracer. After fixation and sectioning, all vascular elements were labeled with another fluorescent tracer. By use of thresholding, a four-color-coded map was presented coding (1) for the intervillous maternal blood space, (2) for trophoblast and fetal non-vascular tissue, (3) for non-perfused or rapidly clearing vessels and (4) for intravitally perfused tracer remaining in the vessel walls or lumen. According to the authors, mapping a series of time-points could define the transfer rates of a specified molecule across each structure in the placental tissue, and thus represents vascular processing by adding a fourth dimension, time, to the three-dimensional analysis.

Four-dimensional imaging of filter-grown epithelial cells was recently addressed by Wakabayashi et al. (2007). Aiming at understanding epithelial polarity, cells were cultured on the underside of a permeable membrane (Transwell) filter. These cells exhibited a fully polarized state but, in contrast to cells cultured on top of filters, were fully accessible for fluorescent quantitative live cell imaging with an inverted microscope because the filter did not obstruct the microscope light path. The authors impressively demonstrated that their approach is an easy reproducible way of investigating living cells in a polarized state in their native environment, allowing selective manipulation of the apical and basolateral surfaces.

A promising method to be used in developmental studies was presented by Reupke et al. (2009). First, the authors stained cell nuclei of the rabbit blastocyst with DNA dyes Hoechst33342 and DAPI, which differently stained nuclei of extraembryonic as well as intraembryonic cells, but did not interfere with normal development up to 10 h in vitro. Multi-photon microscopy settings were further defined for gentle live imaging, and individual cells were ablated by increasing laser energy to a sub-nucleus-size. This led to necrosis in the targeted cell only. These findings encouraged the authors to extend their method for long-term observations and functional investigations in the future.

Molecular quantification techniques and other methodical improvements

Tissue microarrays (TMAs) provide high-throughput histomorphologic tissue examination based on signals obtained with FISH, IHC or other analyses. Conway et al. (2008) reviewed the novel use of virtual slides as a method to replace traditional glass slides with digital images that can be easily be assessed in an automatically and quantitatively manner. The authors described why virtual slide overcomes problems attributable to sampling bias and interpretation of the observer and provided help for the researcher considering implementation of such a workflow solution.

Imaging mass spectrometry (IMS) is a promising approach to focus on morphology and proteomics as well. Walch et al. (2008) reviewed the current state on this topic, focusing on matrix-assisted laser desorption/ionization (MALDI)-IMS. This technique allows identification of protein profiles within a tissue structure. After describing basic principles and integration with histological stainings, the authors gave interesting examples of recent applications, which include comparisons of non-cancerous (exocrine pancreas) and cancerous tissue (invasive ductal pancreatic cancer). In their conclusion, the extensive spatially resolved biomolecular information obtained with MALDI-IMS could lead to a conclusive picture of the molecular processes underpinning biological and pathological processes.

Formalin fixation and subsequent paraffin embedding (FFPE) is the most commonly used method for tissue storage (O'Leary et al. 2009), but this procedure is associated with substantial damage to nucleic acids within these probes. Therefore, analysis of DNA or RNA sequences within these probes remains a challenging endeavor. Farragher et al. (2008) summarized results of recent studies addressing this problem. Interestingly, using both quantitative PCR and microarray profiling, different researchers reported that investigations comparing results from FFPE, and fresh frozen tissue from the same source showed no dramatic differences in gene expression profiles. This led the authors to claim the opportunities of these techniques in the development of a personalized medicine. Another post-processing method for FFPE has been proposed, aiming to retrieve antigenic epitopes that have been masked during formalin fixation (Kajiya et al. 2009). Kajiya et al. (2009)

improved the method of heat-induced epitope retrieval (HIER) focusing on adjusting the buffer conditions during this procedure on the isoelectric points of the antigens of interest. For efficient HIER leading to positive antigen binding, antigens with acidic isoelectric points required basic pH buffer conditions and vice versa. This was exemplified with nuclear antigens comprising human pituitary transcription factors. Consequently, recent work demonstrated that in FFPE, many undiscovered secrets for the cell biologist are still hidden.

Cell biology

Nucleus and nucleolus

The nucleolus contains large DNA loops emanating from ribosomal (r)RNA-coding chromosomal sites to provide transcription of rRNA, which, together with ribosomal proteins, build up the ribosome (Sirri et al. 2008). But many functions of this exciting organelle are still unresolved. Sirri et al. (2008) recently provided an extensive overview on this topic, beginning by describing its compartmentalization into fibrillar centers, the dense fibrillar component and the granular component. The authors further continued with the modulation of rRNA transcription and trafficking/dynamics of the molecular nucleolar actors. By providing links to different associated pathologies (for example concerning protein rev of human immunodeficiency virus 1 which localizes to nucleoli; Cao et al. 2009), the authors finally highlight the importance of nucleolus research for understanding the pathogenesis of important diseases. In this regard, Thiry et al. (2009) reported a detailed investigation on the localization of the nucleolar phosphoprotein Nopp140 within cells during interphase and mitosis. Both immunofluorescence and immuno-EM were used to detect the protein. Signals were detected not only in the dense fibrillar component but also over the fibrillar centers of nucleoli, and also in Cajal bodies, which are spherical suborganelles preferentially found in the nucleus of proliferative cells. During mitosis, Nopp140 organization was lost and the protein dispersed into numerous cytoplasmic foci. Nevertheless, it reappeared in the reforming nucleoli of daughter nuclei. The authors therefore suggest Nopp140 to be a component implicated in the early steps of pre-rRNA processing.

Shin et al. (2008a) analyzed nuclear distribution of polyamines. Polyamines are present in nearly all organisms, and are known to be required for cell growth and differentiation (Thomas and Thomas 2003). Specific polyamine staining was achieved by developing a special pretreatment prior to the immunoreaction. As demonstrated in a variety of cells, polyamines localized to both nucleoli and nuclei, which led the authors to suggest unknown nuclear function of these molecules.

A similar study addressed nuclear localization of actin and actin-binding proteins (Dingova et al. 2009). Adaptor proteins known to be found at cell–cell contacts are beginning to emerge as nuclear players as well, shuttling from membranes to nuclei upon certain stimuli (Hubner et al. 2001). By overlaying immuno-EM data on overall nuclear ultrastructure, nuclear localization of α-actinin, spectrin, tropomyosin, p190RhoGAP and others, together with colocalization of actin with several of these actin-binding proteins was found. This was supplemented with cell fractioning experiments and subsequent Western blotting studies. As multiple proteins that were traditionally found to localize to the cytoplasm only are increasingly found in the nucleus (Kahle et al. 2007), the next steps need to explore nuclear functions of these proteins.

Wide confocal cytometry was presented by Iborra and Buckle (2008) as a powerful approach to study proteomic and structural changes in the cell nucleus during the cell cycle in relationship with structural changes. With the help of a confocal microscope setup, the DNA content allowed the authors to assign a cell cycle stage to individual cells, which were then compared to a protein or DNA marker of the same cell. As an example of the potential of this methodology changes in cell nuclei during the cell cycle were investigated, and potential explanations for this behavior were given.

Nuclear dynamics and trafficking were the subjects of two recent reviews (Lim et al. 2008; Misteli 2008). Protein and RNA trafficking is essential for cellular function and homeostasis. The spatial separation between the cytoplasm and the cell nucleus by the nuclear envelope highlights the nuclear pore complex (NPC) as the only passageway in and out of nuclei. Lim and co-workers summarized recent knowledge on structure and function of NPCs. X-ray or cryo-electron tomography studies have shed an impressive light on the NPC ultrastructure (Stewart et al. 2007; Trinkle-Mulcahy and Lamond 2007), but the authors also focused on functional aspects of these pores. They highlighted groundbreaking biophysical experiments that led to modern models of NPC action, such as the selective phase model by Görlich and co-workers (Frey et al. 2006) or the repulsive action of phenylalanine repeats (Lim et al. 2007). In another review, Misteli (2008) aimed at summarizing current knowledge about intranuclear dynamics. Intranuclear trafficking occurs largely by energy-independent mechanisms, and is driven by diffusion. Several observations showed that dynamic trafficking of proteins and RNA could have regulatory functions such as the regulatory mechanism of intranuclear sequestration. It was therefore proposed that the dynamic nature of proteins and RNAs is emerging as a

tool to control cellular pathways. Adding to this, in a recent investigation, Cisterna et al. (2009) further provided evidence for an active transport mechanism of small ribosomal subunits from the nucleolus to NPCs. They demonstrated that blockade of ATP synthesis and inhibition of the nuclear actomyosin system led to structural and functional modifications of nucleoli. The authors interpreted their data by suggesting that this active mechanism of small ribosomal unit transport is a cellular mechanism which is utilized when a more rapid and directional export is needed.

Peroxisomes

In 2008 and 2009, several reviews were published summarizing the biology and function of peroxisomes. Most of them were presented on the occasion of the 50th symposium of the Society for Histochemistry, the discovery of the DAB method for staining of peroxisomes 40 years ago (Dariush Fahimi 2009; Delille et al. 2009; Karnati and Baumgart-Vogt 2008, 2009; Schrader and Fahimi 2008; Yokota and Dariush Fahimi 2009) and on the 75th birthday of one of the founding fathers of peroxisome research, H. Dariush Fahimi (Schrader 2009). More than half a century of peroxisome research has shed light on this organelle with over 50 associated peroxisomal proteins contributing to essential metabolic processes such as β-oxidation, biosynthesis of phospholipids and metabolism of reactive oxygen species (ROS). In a very personal commentary, Dariush Fahimi (2009) summarized that nearly half a century after the discovery and visualization of peroxisomes, attention to their importance in biomedical research must be drawn. Researchers are beginning to realize peroxisomes as dynamic organelles rapidly assembling and degrading. In a review on the close interrelationship between mitochondria and peroxisomes, both functionality and associated disease conditions were highlighted (Delille et al. 2009). The role of peroxisomes in pulmonary biology was addressed by a recent study and an overview by Karnati and Baumgart-Vogt (2008, 2009). Regulation of lipid homeostasis and pulmonary surfactant layer is known to lead to protection of inner pulmonary surface epithelia against oxidative stress. The authors used a variety of methods including fluorescence and electron microscopies as well as biochemical techniques and focused on different peroxisomal marker proteins (for example Pex13p, β-oxidation enzymes and catalase). In contrast to previous reports, the authors reported that peroxisomes are highly abundant in the bronchiolar epithelium, with particular species differences between man and mice. Finally, Angermuller et al. (2009) focused on the connection between peroxisomes and ROS, because these organelles possess the key enzymes generating and scavenging H_2O_2. The authors inspiringly noted "an organelle once termed a fossil proves to be highly vivid and is still a challenging and demanding subject of scientific research".

Lipid droplets

In the overview article by Fujimoto et al. (2008), an extensive summary of research on lipid droplets (LDs) was provided. LDs were once thought to be sole depots of neutral lipids existing in nearly every cell. Recent studies, however, have highlighted additional roles of LDs besides contributing to lipid homeostasis. These include the temporal storage for lipidated proteins and even histones in the Drosophila embryo (Cermelli et al. 2006). Further topics addressed morphology, molecules, biogenesis and related diseases of LDs, the latter including lipodystrophies or hepatitis C virus infections (see also the recent study by Roingeard et al. 2008). In a more recent work of the same group (Cheng et al. 2009), the authors reported a new method for studying triglyceride incorporation into LDs. While aiming at elucidating LD growth processes, a novel EM method quantifying the proportion of existing and newly synthesized triglycerides was presented. This method used the reactivity of unsaturated fatty acids with osmium tetroxide the binding specificities of which have been explored in detail by Belazi et al. (2009). The authors found that newly synthesized triglycerides were incorporated to a highly uniform rate into existing LDs, which, together with the noninvolvement of microtubules in this process, indicated that triglycerides are synthesized and incorporated in close vicinity of single LDs. In a study by Diaz et al. (2008), an increase in LD numbers has been found in proliferating fibroblasts. The authors used Nile red staining and positive immunostaining with adipophilin but not perilipin as a marker system for LDs. LD numbers in proliferating cells correlated with DNA content which led the authors to suggest a continuous accumulation of LDs during cell growth. Changes in both the number and composition of LDs were also found in growing cells treated with inhibitors of cholesterol esterification. The work of Shaw et al. (2008) focused on establishing a combination of fluorescent stains allowing visualization of both mitochondria and LD networks in human skeletal muscle fibers by CLSM. Antibodies against cytochrome *c* oxidase clearly marked mitochondrial networks, whereas oil red O visualized LDs. In another study, the authors further used their method to analyze adipophilin distribution in skeletal muscle (Shaw et al. 2009), showing that this LD-associated protein is located in the areas located between the mitochondrial networks. Moreover, the authors showed that intramyocellular LDs consist of a heterogeneous pool of adipophilin-positive and -negative droplets.

Centrosomes

Centrosomes are primary microtubule-organizing centers of mammalian cells (Alieva and Uzbekov 2008), but a recent review extended its roles to cell growth and organization (Schatten 2008). This organelle is now known to orchestrate entry into mitosis and several other mitotic steps, while also monitoring DNA damage. In this context, a scaffolding function for kinases and phosphatases coordinating multiple cell cycle-specific functions has to be mentioned. The authors critically pointed out the involvement of centrosomes in disease conditions ranging from cancer to neurological disorders. Another work identified Nedd1 as a novel centrosomal marker during mouse embryonic development (Manning et al. 2008). Nedd1 has been shown to localize to centrosomes and spindles by interacting with γ-tubulin and γ-tubulin complex proteins (Manning and Kumar 2007). The authors applied this marker to study centrosomes in highly proliferating cells during neural development and found it to localize in the developing lens, retina and other polarized tissues. Functional roles for these processes, however, are still lacking.

In contrast to other cells, microtubules in neurons adopt unique arrangements, since most of these structures are not attached to the centrosome (Yu et al. 1993). Ohama and Hayashi (2009) therefore examined dendritic localization of the centrosomal protein ninein. Ninein has microtubule-anchoring and stabilizing functions. In immunohistochemical analyses, ninein signals at centrosomes in undifferentiated neural precursors were demonstrated. This localization was lost in migrating and differentiated neurons, such as pyramidal neurons of the cerebral cortex. Here, ninein was diffusely present in both cell soma and dendrites. Triton extractions and experiments using nocodazole treatment to disrupt microtubule patterns in cultured neurons confirmed the microtubules-anchoring and stabilizing function of ninein in dendrites.

Endoplasmic reticulum, secretory pathways and vesicular trafficking

Various reviews summarized recent research on intracellular vesicular trafficking involving the Golgi network, endoplasmic reticulum (ER), exosomes as well as endosomes and endo-lysosomes (Hughes and Stephens 2008; Lavoie and Paiement 2008; Luini et al. 2008; Pavelka et al. 2008; Roth et al. 2008b).

The quality of newly synthesized proteins is extensively monitored to sustain proper folding and correct assembly in the early secretory pathway, the cytosol and the nucleoplasm. In their recent review, Roth et al. (2008b) addressed the cellular machineries of protein quality control. The authors focused on ER-associated degradation, or degradation of misfolded glycoproteins involving glucosidase II and UDP-glucose:glycoprotein glucosyltransferase in connection with the calnexin/calreticulin cycle. Also, novel approaches of treating diseases associated with misfolded proteins, such as open angle glaucoma and Fabry's disease caused by myocilin and α-galactosidase A mutations, respectively, by using synthetic chaperones were presented.

The review by Luini et al. (2008) focused to depict and understand the key players in trans-Golgi network-based sorting and delivery process, the so-called post-Golgi carriers (PGCs). The PGC lifecycle was illustrated which included the formation of trans-Golgi tubular export domains, the docking of these tubular domains onto molecular motors and their extrusion toward the cell periphery. This normally leads to fission of the forming PGC and the delivery to its targeted organelle. Another review summarized current knowledge about the trafficking of molecules that escaped from their compartments of function (Pavelka et al. 2008). This so-called retrograde traffic in the biosynthetic-secretory route plays essential roles keeping the compartments' balances and maintenance of the functional integrities of organelles. Internalized molecules may be transported in retrograde direction along the secretory route, which is sometimes misused by pathogenic bacterial toxins such as Shiga toxin. The authors illustrated how these insights into retrograde trafficking helped to develop strategies for targeted intracellular delivery of drugs. Moreover, contradicting results regarding these complex pathways were mentioned questioning the already established traffic models.

Hughes and Stephens (2008), in another excellent and extensive review, unraveled the structure and function of the COPII coat. This multi-subunit complex is essential for the secretion of proteins or macromolecules from the secretory pathway to the extracellular space. Here, traditional studies of yeast genetics and biochemical reconstitutions are summarized together with findings from clinical cases as well as modern genetics. The insights into molecular key players for this machinery came clearly into view with the explanation of associated diseases such as cranio-lenticulo sutural dysplasia, which results from a missense mutation in Sec23A, one of the multiple proteins forming the COPII subunits.

A detailed review on the function of ER molecular machines besides the COPII complex was given by Lavoie and Paiement (2008). These included chaperones, Ca^{2+}-handling proteins, enzymes of lipid and glucose metabolism or detoxification, antigen processing proteins and finally cytoskeletal or signaling proteins.

LDL receptor-related protein 9 (LRP9) is a distant member of the low-density lipoprotein receptor (LDLR) superfamily and was found to be associated with trans-Golgi network and endosomes in a recent study by Boucher et al.

(2008). By using different mutant constructs and CLSM, the authors emphasized that this localization was dependent on the presence of two acidic cluster/dileucine (DXXLL) motifs in the cytoplasmic tail of LRP9. These motifs were found to interact with the Golgi-localized, γ ear-containing ADP ribosylation factor binding proteins, which are clathrin adaptors involved in transport between the Golgi and endosomes.

The work of Vivero-Salmeron et al. (2008) extensively characterized the (tubular) connections between different compartments of the secretory pathway by applying detailed ultrastructural investigations using EM and cryo-immunocytochemistry (cryo-ICC). By using different markers such as PDI, COPII, KDEL receptor, giantin or Rab6, transient continuities throughout the secretory pathways were reported as a main outcome.

Heat shock proteins (HSPs) are known to be molecular chaperones facilitating protein folding or translocation and recognition of misfolded proteins. The expression pattern of HSPa2 in mouse tissues was addressed by Vydra et al. (2009). In accordance to its original name and origin (testis-specific HSP70), high amounts of HSPa2 were found in germ cells by Western blotting or immunohistochemical studies. But HSPa2 0 was also produced in various other epithelial cells in bronchioles, oviduct, endometrium, thymus, urinary bladder or ependymal cells. These findings led the authors to speculate on specific roles of this chaperon in these tissues.

Xu et al. (2009b) demonstrated in their recent study that, although having only minor differences in the amino acid sequence, human signal peptide led to increased secretion of a fusion construct into the cell culture supernatant of transfected NIH3T3 cells, compared to the mouse signal peptide counterpart. This finding could be adopted by researchers trying to increase secretion of fusion proteins of non-human origin.

Endocytosis, caveolae, lysosomes and autophagy

Van Meel and co-workers provided an extensive review on lysosomes, which are named after the Greek words for lytic body. Lysosomes are known to be specialized organelles for the degradation of endocytosed material, which may enter the cell by clathrin-dependent and independent pathways (Saftig and Klumperman 2009; Sandvig et al. 2008), and intracellular material, which has passed to the autophagy pathway (Uchiyama et al. 2008). Consequently, lysosomes are essential regulators of cellular homeostasis. Van Meel and co-workers focused not only on sorting and transport within the endo-lysosomal pathways but also gave a historic overview on the discovery of lysosomes, which according to the authors was a compelling detective story. Throughout their review, they highlighted their summaries with EM images that made invaluable contributions to our understanding of the endo-lysosomal system today. Kurz et al. (2008) extended this work with a review addressing lysosomes in iron metabolism, aging and apoptosis. As many macromolecules contain iron, lysosomal degradation of these molecules leads to an iron-rich environment in lysosomes. This makes them sensitive to oxidative stress because of Fenton-type reactions that take place in the presence of redox-active iron, which finally leads to production of ROS. The authors discussed how the magnitude of oxidative stress determines the degree of lysosomal destabilization and the resulting initiation of consequences such as apoptosis or necrosis, and they also refer to various lysosomal storage- and aging-associated diseases. Endo-lysosomal degradation of epidermal growth factor receptor (EGFR) is known to be a physiological mechanism in EGFR signaling (Sebastian et al. 2006). Impaired EGFR degradation, however, has often been associated with cancer. Roepstorff et al. (2008) reviewed current research on this topic, and discussed how targeted anti-cancer therapies are using these processes.

Besides these overviews, several original articles shed new light onto the endocytotic machinery. Bogdanovic et al. (2009) studied tyrosine kinase receptor Tie2, which is expressed on endothelial cells and targeted by its ligand angiopoietin-1. Tie2 has been attributed important functions for angiogenesis and vascular stability. Immuno-EM depicted variably sized Tie2 clusters on the surface of endothelial cells. Angiopoietin-1-induced activation led to Tie2 colocalization with clathrin-coated pits. Although knockdown of clathrin heavy chains did not result in protection against angiopoietin-1-induced endocytosis, inhibition of cellular endocytosis by several pharmacological approaches blocked the internalization of Tie2 in response to angiopoietin-1. These findings were interpreted by the authors that one pathway mediating the internalization of Tie2 in response to angiopoietin-1 is mediated by clathrin-coated pits.

Endocytosis involving caveolae, which are flask-shaped plasmalemmal vesicles, were investigated in a recent work by Berg et al. (2009). With the help of fluorescent microscopy, EM and different staining protocols, the authors demonstrated that internalized caveolae clusters in fibroblast-like synoviocytes represent a rather static compartment contacted by vimentin filaments. Caveolae association of RECK, a glycosylphosphatidylinositol-anchored protein acting as a negative regulator of cell surface metalloproteinases, was also reported in these cells, leading the authors to speculate about the roles of these proteins in static clusters of caveolae.

An article by Wustner and Faergeman (2008) described the visualization of dynamic processes of sterol endocytosis and its associated changes in plasma membrane sterol

distribution in living mammalian cells. The authors applied UV-sensitive wide field microscopy of two intrinsically fluorescent sterols, dehydroergosterol and cholestatrienol, combined with advanced image analysis. Experiments using cells expressing GFP fused to caveolin-1 indicated that the internalization of at least a part of these fluorescent sterols is mediated via caveolae-dependent endocytosis. Nevertheless, sterol endocytosis did not require formation of microscopically resolvable sterol clusters or enrichment of sterols in caveolae.

Cell junctions and communication

Organization of cells into tissues and higher order structures strictly necessitates the establishment and regulation of cellular junctions. These formerly assumed static structures are now emerging as dynamic multiprotein complexes involved in physiological and pathophysiological processes as well as in cellular signaling (Ebnet 2008). Several paramount reviews have summarized current knowledge about desmosomes (Waschke 2008), tight junctions (TJ) (Forster 2008), gap junctions (GJ) (Prochnow and Dermietzel 2008) and adherens junctions (AJ) (Rudini and Dejana 2008).

Ionic concentrations are essential for auditory functions in the cochlea. Glucose metabolism plays an important part as well. Suzuki et al. (2009b) now demonstrated that GJs together with glucose transporter 1 (Glut1) mediate intercellular glucose transport in the rat cochlea. IHC as well as glucose imaging using a fluorescent glucose analog showed presence of Glut1 as well as of GJ proteins connexin (Cx)26 and 30 and distribution of glucose throughout the stria vascularis and spiral ligament, which could be blocked by GJ inhibition. The authors suggested that GJs mediate glucose transport from Glut1-positive cells (strial basal cells) to Glut1-negative cells (fibrocytes in the spiral ligament and strial intermediate cells) in the cochlea.

Transport and interactions of GJ protein Cx43 along the secretory pathway has been studied by Majoul et al. (2009). They focused on small GTPases and used GFP-variant-tagged proteins in their experiments. GTP-restricted Sar1 arrested Cx43 in COP II-coated ER exit sites and accumulated 14-3-3 proteins. This suggested that Cx43 already existed in an oligomeric state at ER exit sites, which was confirmed by FRET-FLIM experiments. Moreover, GTP-restricted Arf1 blocked Cx43 in the Golgi and GTP-restricted Arf6 removed Cx43 plaques from the cell–cell interface leading to their degradation. All in all, interesting insights into regulation of Cx43 by small GTPases in the secretory pathway have been presented, which were discussed in the context of facilitation or interruption of cell–cell communication through GJs.

Novel data on TJ proteins in formation of bile canaliculi have been reported by Son et al. (2009). TJs are important for sealing the paracellular barrier in epithelial and endothelial cells (Forster 2008). Occludin and members of the claudin protein family constitute the TJ strands. TJs are known to separate polarized hepatocytes by the formation of sinusoidal (basolateral) and bile canalicular (apical) plasma membrane domains. To investigate the role of the integral TJ protein claudin-2 in bile canalicular formation, Son and co-workers used a knockdown approach to abolish claudin-2 expression by siRNA. Knockdown of claudin-2 prevented bile canalicular formation, dramatically changed hepatocyte phenotype and led to alterations in several cellular signaling cascades. These findings were interpreted to support the hypothesis that claudin-2 may not only affect the bile canalicular seal but also its formation. Insights into the role of TJ proteins and ZO-1/2 in pathologic conditions of increased biliary permeability were added in another study (Maly and Landmann 2008). Bile duct ligation in rats was found to cause upregulation of ZO-2 and decreased colocalization of claudins with ZO-1 and occludin leading the authors to conclude that differential expression these proteins has functional implications for bile formation, confirming the other report (Son et al. 2009). In three recent studies, Inai and co-workers analyzed TJ proteins of the claudin family (Inai et al. 2008, 2009; Sengoku et al. 2008). In their first study (Inai et al. 2008), they compared claudin isoforms and TJ morphology in two different mouse rectum cells (CMT93-I and -II), because these cells were found to either lack or express claudin-2. Expression of other claudins appeared normal in these cells. However, transepithelial electric resistance (TER) measurements revealed higher resistance in CMT93-I compared to CMT93-II monolayers. Their findings provide a first indication that expression of claudin-2 may be related to decreased TER. In the second study (Inai et al. 2009), the authors investigated the role of highly conserved amino acid residues “FY” and “PL” in the second extracellular loop of classic claudins for the formation of TJ strands in TJ-free HEK293 cells and TJ-bearing MDCK II cells. Mutant constructs lacking these amino acid residues coupled to EGFP-variant fusion proteins and subsequent CLSM as well as freeze-fracture EM demonstrated that mutant proteins still could form TJ strands in TJ-free HEK293 cells. Differences in TJ-bearing MDCK II cells existed suggesting that endogenous claudins in these cells accounted for these differences. In a third manuscript, the authors explored TJ formation in MDCK II cells in response to claudin-15 overexpression (Sengoku et al. 2008). By applying similar techniques as in their previous studies, it was shown that overexpression of claudin-15 induced aberrant strands in MDCK II cells. The authors noted that investigating the process of aberrant TJ formation may lead to clues for normal TJ assembly.

In a study by Uehara and Uehara (2008), the authors focused on splenic sinus endothelial cells joined by TJ and

AJ, because these cells regulate the paracellular passage of blood cells thorough the spleen (Groom et al. 1991). In immunofluorescent and immunogold studies, the localization of claudin-5, TJ-associated protein ZO-1 and α-catenin in rat spleen sinus endothelial cells of tissue cryosections was examined. Positive signals of all three proteins were found with the proteins closely localizing along the junctional membranes of adjacent endothelial cells.

Wolburg et al. (2008) investigated the expression pattern of water channel proteins aquaporins (AQPs) as well as TJ proteins in the olfactory system of the rat. They used glial olfactory ensheathing cells (OECs), which are promising candidates to support nerve injury regeneration. By means of freeze-fracturing and ICC, no indications for AQPs, but immunoreactivity for ZO-1, occludin, and claudin-5 was demonstrated. The latter results were compared to permeability and TJ composition of blood vessels and fila olfactoria, which were found immunopositive for ZO-1 and claudin-5. A detailed study of junctions and their molecular composition in the olfactory epithelium of the rat was provided by Steinke et al. (2008).

A novel way of intercellular communication was reviewed by Gurke et al. (2008). Tunneling nanotubes were discovered recently (Rustom 2009) and demonstrated to be based on de novo formation of membranous F-actin-rich structures between cells. These structures were identified in various cell types, including pheochromocytoma cells, HEK293 cells or astrocytes. Indications for the in vivo existence of these structures and functional roles in cargo transport were given.

An extreme condition of cell communication is the process of cell fusion. This was also the topic of a recent review by Larsson et al. (2008). The importance of this process in various physiological conditions, which include fertilization, placentation, development of skeletal muscle and bone, Ca^{2+} homeostasis, the immune defense system and cancer development, was highlighted and elaborately described. Especially in the context of cancer, the syncytin family of proteins has been reported to function as fusogens placing them as upstream regulators of the cell fusion machinery (Larsson et al. 2007).

Cell cytoskeleton

The cytoskeleton is a cellular scaffold inside the cytoplasm and mostly consists of actin, intermediate filaments (IFs) and microtubules (Erickson 2007). Extensive reviews have summarized the role of one of the most abundant cytoskeletal proteins in eukaryotic cells, i.e. actin (Schleicher and Jockusch 2008), the function of epithelial IFs (keratins) in physiological and diseased conditions (Moll et al. 2008; Strnad et al. 2008) and the structure and functions of microtubules in mammalian cilia (Satir and Christensen 2008).

Apoptosis

Molecules specifically marking and determining the programed cell death are becoming to emerge as essential tools in investigating apoptotic processes. Although originally defined by structural alterations, a wide variety of imaging and biochemical techniques are available for the identification of apoptotic processes, and special emphasis is put on the different modes of apoptosis induction (Hengartner 2000; Taatjes et al. 2007, 2008a).

Extending a previous study (Brandt et al. 2008), Lange et al. (2009) recently provided an interesting observations on apoptosis induction in the T cell model of Jurkat T lymphocytes. They focused research on galectin-1, which triggers T cell death via apoptotic death receptor activation (Hasan et al. 2007). Downstream of activation of the death-receptor pathway, galectin-1 was found to mediate apoptosis via the mitochondrial pathway in Jurkat cells. As a critical part of the latter pathway, galectin-1, in a caspase-8 dependent manner, induced proteolytic cleavage of Bid, a member of the Bcl-2/Bcl-xL family resulting in mitochondrial cytochrome *c* release. As later markers of apoptosis, cleavage of DNA-repair enzyme poly (ADP-ribose) polymerase or nuclear lamin A as substrates of activated caspases was found. These results placed Bid as a connection between the death receptor and the mitochondrial pathway of galectin-1-induced apoptosis in human Jurkat T lymphocytes.

In a series of articles, Bottone and co-workers addressed photosensitization in response to Rose Bengal acetate (RB-ac) (Bottone et al. 2007, 2009; Soldani et al. 2007). RB-ac induces multiple organelle photodamage followed by apoptotic cell death, which is especially interesting as the treatment against tumor cells. Tumor-sensitive photosensitizing agents combined with light irradiation at activating wavelengths could be used to specifically ablate pathogenic cells. In their recent work (Bottone et al. 2009), the authors further explored the mode of action of RB-ac and found both activation of caspase-dependent and caspase-independent apoptotic pathways. Their findings were interpreted to place RB-ac as a promising and powerful cytotoxic agent in photodynamic therapy.

Specific cells and tissues

Muscle

Skeletal muscle

In two recent studies investigating effects of long-term bed rest on expression of different Ca^{2+} homeostasis markers in myofibers, Salanova et al. (2008, 2009) took advantage of a

60-day horizontal bed rest study of human volunteers without or with exercise countermeasure (resistive vibration exercise). In the first investigation, changes in sarco/endoplasmic reticulum Ca^{2+} ATPase (SERCA) isoform expression and S-nitrosylation in myofibers of lower limb soleus and vastus lateralis muscle biopsies were investigated (Salanova et al. 2009). After bed rest, a subpopulation (~15%) of slow myofibers additionally expressed the fast SERCA1a isoform in control but not in exercised volunteers. SERCA1a S-nitrosylation decreased in unused soleus muscles but in response to exercise increased in both muscles suggesting specific responses to exercise in different muscles. In the other report, the focus laid on the ryanodine receptor type-I (RyR1) as a key part of the excitation–contraction coupling machinery (Salanova et al. 2008). In the bed rest group, decreased RyR1 immunofluorescence intensity and ryanodine binding were found. After exercise, however, RyR1 immunosignals as well as ryanodine binding increased leading the authors to conclude that exercise countermeasures maintained normal RyR1 levels during prolonged bed rest. SERCAs and RyR have also been studied by an Italian group of researchers recently. Giacomello and Sorrentino (2009), however, focused on the differential expression of the muscle-specific isoform of ankyrin1 (Ank1.5) and its giant interacting partner obscurin and the above mentioned Ca^{2+} channels in developing sarcomers. Localization of Ank1.5 at Z-disks in E14 muscle fibers revealed that Ank1.5 is among the earliest sarcoplasmic reticulum proteins to assemble, even preceding SERCA and RyR. Obscurin immunostainings were detected at the Z-disk and M-band, but with differences between pre- and after birth conditions. Because these differences were detected with two antibodies directed against the N- or C-terminus of obscurin, the authors concluded that exposure of obscurin epitopes changes during skeletal muscle development. Another study had been intended to extend and clarify the differential expression of obscurin during muscle development (Carlsson et al. 2008). The authors precisely localized obscurin in developing and mature human striated muscle, and showed that it is surrounding myofibrils at the M-band level in both stages. At maturity, obscurin also linked peripheral myofibrils and the sarcolemma, and was identified to be a component of the neuromuscular junction. The authors gave a detailed classification of obscurin as an additional member of the extrasarcomeric cytoskeleton, and also successfully tested this function in a model for sarcomerogenesis confirming another study (Borisov et al. 2008).

The ankyrin-repeat protein with a PEST motif and a proline-rich region (Arpp) as a member of the muscle ankyrin repeat proteins has been studied by Tsukamoto et al. (2008). They applied a muscle injury model to focus on Arpp's role in muscle stress responses and its potential nuclear shuttling ability. Nuclear accumulation of Arpp in euchromatic regions was found in damaged myofibers. This led the authors to speculate that Arpp may act in response to muscle stress by regulating gene expression, for example by interaction with p53, which has been reported before (Kojic et al. 2004).

Low et al. (2009) studied the expression of sodium/ascorbate co-transporter SVCT2 in slow-twitch skeletal muscles of the chick. Although skeletal muscle contains about the half of the whole-body vitamin C, the expression of SVCT transporters has not been clearly addressed. Immunohistochemical analyses revealed that SVCT2 was preferentially expressed by type I slow-twitch muscle fibers throughout chick myogenesis as well as in postnatal skeletal muscles of several species, including human.

Jocken et al. (2008) documented the expression of adipose triglyceride lipase (ATGL) in human skeletal muscles. The authors found that ATGL expression is type I (oxidative) fiber specific. This was confirming an interesting prior finding that ATGL-deficient animals show significant lipid accumulation in skeletal muscle. Because of its special expression in oxidative fibers only, the authors speculated on a pivotal role of ATGL in intramuscular fatty acid homeostasis.

Recent research suggested that estrogen receptors (ERs) have important functions in skeletal muscles. After a study in pigs had been published (Kalbe et al. 2007), Wiik et al. (2009) recently characterized ERα and ERβ expression in human skeletal muscle biopsies taken from vastus lateralis by ICC. Both ER isoforms were localized in all subjects, including postmenopausal women, and no sex differences were observed. The authors proposed that their findings were the first to demonstrate age- and sex-independent expression of ERα protein in human skeletal muscle.

Cizkova et al. (2009) reported the expression of nestin, desmin and vimentin in intact and regenerating muscle spindles of rat skeletal muscles. They used a model of muscle spindle regeneration by intramuscular isotransplantation of extensor digitorum longus muscle from 15-day-old rats into the muscle of adult female inbred Lewis rats. After an endpoint of 7-, 16-, 21- and 29-day survival, muscle tissues were immunohistochemically stained. In contrast to intact host spindles, nestin expression was found in regenerating spindle fibers, but was lost after 21 days. Desmin was detected in spindle fibers at all developmental stages in regenerating as well as in intact spindles. Vimentin was expressed in cells of the outer and inner capsules of all muscle spindles and in newly formed myoblasts and myotubes of regenerating spindles 7 days after grafting. The authors' findings indicated that these IFs act as small-diameter extrafusal fibers, confirming their prior reports.

Switching of actin isoforms from α-cardiac to α-skeletal actin occurs during skeletal muscle differentiation (Lin and

Lin 1986). By using cultivated mouse embryonic stem cells, this switching of actin isoforms was demonstrated by Mizuno et al. (2009) for the first time in vitro. Only after myotube formation, the cardiac type actin decreased and α-skeletal actin increased and remained as the main actin component in mature skeletal muscle. This study demonstrated the useful approach of in vitro embryonic stem cell differentiation for exploring skeletal muscle differentiation.

A new multiple labeling method to identify satellite cells in human muscles has been reported by Lindstrom and Thornell (2009). The authors took advantage of simultaneously monitoring two satellite cell markers (NCAM and Pax7), the basal lamina and nuclei. They tested their procedure on biopsies from power-lifters, power-lifters using anabolic substances and untrained subjects. Three subtypes of satellite cells were identified: NCAM(+)/Pax7(+) (94%), NCAM(+)/Pax7(−) (4%) and NCAM(−)/Pax7(+) (1%), but large individual variability existed. However, the proportion of satellite cells per nuclei within the basal lamina of myofibers was similar for all groups reflecting a balance between the number of satellite cells and myonuclei. The authors recommended the use of their multiple marker method for more reliable satellite cell identification and quantification.

Smooth muscle

CPI-17 is an inhibitor for myosin light chain phosphatase and consequently participates in Ca^{2+} sensitivity of smooth muscle contraction. Kim et al. (2009a) now analyzed CPI-17 immunoreactivity during embryonic smooth muscle development and also lesion formation of arterial neointima. Like α-actin and other smooth muscle markers, CPI-17 was expressed in embryonic heart, but was downregulated at E17. In injured adult rat neointima, CPI-17 expression levels were also reduced to 30%. Interestingly, CPI-17 immunoreactivity was detected at non-smooth muscle organs in the mouse embryo, such as embryonic neurons and epithelium.

Renegar et al. (2009) compared cellular localization of the proline-rich actin binding protein fesselin in chicken smooth, skeletal and cardiac muscle tissues. Western blot analyses detected large amounts in gizzard smooth muscle, whereas immunostainings revealed the localization as discrete cytoplasmic structures. However, no colocalization with caveolar regions of the cell membrane was detected. Immuno-EM established localization of fesselin within dense bodies, which are anchorage points for actin and desmin in smooth muscle cells.

Connective tissue: teeth, cartilage and bone

Pleitrophin is a secreted, extracellular matrix (ECM)-associated growth factor, which has been suggested to be important for the development of the nervous system and skeleton. Mittapalli et al. (2009) comprehensively characterized pleitrophin expression in the chick embryo until embryonic day 10. ISHs revealed novel expression domains in developing somites and during limb formation and prominent expression in the somitocoel cells of epithelial somites and in a sclerotomal subcompartment, the syndetome. This compartment gives rise to the axial tendons in the vertebral motion segment. In the limbs, pleitrophin was markedly expressed in tendon anlagen and in phalangeal joints. The findings suggest pleitrophin as a novel marker gene in avian somite and tendon development.

Tendons and ligaments possess low healing capacity, but are often affected by mechanical injuries. In their recent study, Tempfer et al. (2009) hypothesized that perivascular tendon capillary cells function as progenitors for functional tendon cells. Immunohistochemical characterization of human biopsies as well as RT-PCR and Western blotting were performed to demonstrate that perivascular tendon capillary cells express both tendon- and stem cell-like characteristics. This was confirmed in in vitro studies using cultured perivascular cells. These findings strengthened the hypothesis of precursor cells residing in perivascular niches and may open potential therapeutic applications.

Odontoblasts are responsible for dentin formation in teeth. Sato et al. (2009) investigated the synthesis and intracellular transport of the most important component of dentin, type I collagen, during odontoblast differentiation. Using IHC and ISH, the authors especially focused on odontoblast processes reaching into the dentinal tubule as a mechanism for protein transport. The level of collagen I mRNA expression decreased during dentinogenesis, whereas the intracellular localization of type I procollagen in odontoblast processes increased significantly with aging. Loss of occlusion caused a significant decrease in type I procollagen.

Rodent incisors are continuously growing teeth performing all stages of odontogenesis, including amelogenesis and dentinogenesis. In their recent work, Lee et al. (2009) explored mitogen-activated protein kinase (MAPK) signaling during incisor development and growth in the mouse. By using pharmaceutical activation and inhibition of MAPKs in in vitro cultures, important functions of MAPKs for amelogenesis were found, which were partly involving Hsp25 signaling activated by phosphorylated ERK and MEK. Hsp25 has been reported to act as a switch between cell proliferation and differentiation during tooth development, which had been characterized in detail in a recent study (Harada et al. 2008).

The role of a member of the disintegrin and metalloproteinase (ADAM) family, ADAM28, in differentiation of human dental papilla mesenchymal cells was the topic of a recent work by Zhao et al. (2008). After confirming ubiquitous

expression of ADAM28 in multiple human dental mesenchymal and epithelial cells, the authors worked with overexpression and antisense constructs. Overexpression of ADAM28 favored the proliferation and lineage-specific differentiation of human dental mesenchymal cells, while inhibition of ADAM28 exerted opposite effects, finally leading to apoptosis. These results provided a first background for an important function of ADAM28 as positive regulator of growth and differentiation during tooth organ development.

For cartilage tissue engineering, chondrocytes isolated from different animal species are used because of the lack of sufficient human cartilage donors. In their recent study, Schulze-Tanzil et al. (2009) investigated in vitro expanding capacities and further characterized various chondrocyte cultures from different species, including equine, porcine and human chondrocytes. Indeed, profound differences in proliferation rates and synthesis of ECM proteins were detected. The authors concluded that porcine chondrocytes share the most similarities to human cells, hinting to important considerations for animal tissue engineering. Aging of chondrocytes of human thyroid cartilage was the subject of a recent study by Claassen et al. (2009). It has been known before that laryngeal cartilages exhibit gender-specific aging, with the female thyroid cartilage remaining unmineralized until high age. The authors now extended these investigations with a profound characterization of apoptosis in these tissues by applying immunohistochemical stainings and EM. As a general finding, apoptotic chondrocytes decreased in thyroid cartilages of both genders with age. However, in the age group of 41–60 years, thyroid cartilage from male specimens revealed a significantly higher percentage of apoptotic cells than thyroid cartilage from women. Taken together, the authors assumed that some chondrocytes in thyroid cartilage die by apoptosis and discuss a possible influence of sexual hormones on apoptotic death of thyroid cartilage cells.

Smith et al. (2009) were interested in the topographical variation of several cartilage proteoglycans in the fetal human spine. The authors elevated the immunohistochemical distribution of aggrecan, versican and perlecan compared to collagen subtypes in the developing human spine of first-trimester fetuses. The authors reported that versican (V0 isoform) was only expressed in the developing intervertebral disk interspace, whereas aggrecan and perlecan also localized in the cartilaginous vertebral body rudiments. Their findings led the authors to speculate that a finely balanced interplay between various proteoglycans and collagens and the spinal cell populations exist, which is important during spinal development.

Several studies focused on mesenchymal stem cells and their differentiation potential, because these cells may be therapeutically used in regenerative medicine (Ben David et al. 2008; Csaki et al. 2007, 2009; Karaoz et al. 2009; La Rocca et al. 2009). La Rocca et al. (2009) isolated Oct-4/HLA-G-positive mesenchymal stem cells from the human umbilical cord matrix via a new protocol, and further characterized this cell population. These cells could undergo several population doublings in vitro and were differentiated into mature mesenchymal tissues such as bone and adipose tissue. Purification of these cells out of the umbilical cord may be a promising tool in regenerative medicine. Karaoz et al. (2009) focused on mesenchymal stem cell derived from rat bone marrow and intensively characterized these cells by applying IHC and RT-PCR studies. Their results led the authors to speculate that these cells can be easily differentiated into multiple lineages. Another set of papers used canine mesenchymal stem cells (Csaki et al. 2007, 2009). By coculture with primary bone-derived osteoblasts, the authors successfully induced osteogenic differentiation in these stem cells, which was confirmed by ultrastructural investigations as well as immunoblotting with osteogenic markers. Ben David et al. (2008) demonstrated that in advanced stages of mesenchymal stem cell-derived osteoprogenitors, exposure to pro-inflammatory cytokines upregulated matrix metalloproteinase (MMP)-9 but not MMP-2. Besides mesenchymal stem cells, another source of osteogenic precursors has been reported for non-adherent bone-marrow-derived mononuclear cells (Suda et al. 2009). These cells can also be obtained by protocols using adherence to plastic surfaces of tissue cultures. Leonardi et al. (2009) derived late adherent subpopulations of non-adherent cells by subsequent replating steps. About one-third of these non-adherent cells showed late adherent behavior and displayed antigens similar to mesenchymal stem cells. The authors speculated that these subpopulations represent a reservoir of osteoprogenitors, which could be used in adequate amounts in tissue engineering strategies.

Neural tissue

In a detailed review, Zimmermann and Dours-Zimmermann (2008) gave a detailed account on recent insights into the role of the ECM for the nervous system. The authors introduced the most important players, including hyaluronan, chondroitin sulfate proteoglycans (aggrecan, versican and neurocan) and tenascins, and highlighted how these molecules can regulate cellular migration and axonal growth during neural development. Another focus lay on the putative role of chondroitin sulfate proteoglycans in suppressing central nervous system regeneration after lesions and potential therapeutic application of chondroitin sulfate-degrading enzymes for partial recovery of lesioned nerves.

Sango et al. (2007, 2008) investigated the protective function of ciliary neurotrophic factor (CNTF) for cultured

adult rat dorsal root ganglions, thereby extending a previous investigation. Recombinant CNTF enhanced survival and neurite outgrowth of cultured rat dorsal root ganglion neurons, and displayed higher efficacy for the promotion of viable neurons and neurite-bearing cells as compared to other neurogenic agents. Biochemical investigations revealed phosphorylation of STAT3, Akt and ERK1/2 in the neurons after application of CNTF, and pharmacological inhibition studies confirmed these findings.

The mollusk abalone was the animal model of a recent study by Panasophonkul et al. (2009). In this model system, the authors investigated expression of a truncated serotonin (5-HT) receptor gene in neural and reproductive tissues, because the neurotransmitter 5-HT has been linked to a variety of biological roles, including gamete maturation and spawning (Turlejski 1996). A potential cDNA encoding a putative 5-HT receptor consisting of 359 amino acids was cloned and shared G-protein-coupled receptor motifs with metazoan 5-HT receptors. However, the third intracellular loop of this receptor was relatively short, and only six transmembrane domains were predicted leading the authors to speculate on a truncated receptor. RT-PCR and ICC studies showed that mRNA of this receptor was present in neural ganglia and gonad tissues. The authors added that the functional relevance of this receptor needed to be verified in future studies.

Mutations in the Lgi1 protein promote the autosomal dominant lateral temporal epilepsy (Michelucci et al. 2009). The exact function of Lgi1, however, is still unknown. Malatesta et al. (2009) now investigated the distribution of the epilepsy-related Lgi1 protein in rat cortical neurons. By combining biochemistry, IHC and immuno-EM, the authors showed that Lgi1 is a cytoplasmic protein distributed in all parts of neurons; it localized on the rough ER, in the Golgi complex and in close proximity to neurofilaments. This led the authors to hypothesize on an association of Lgi1 with axonal cytoskeletal structures for directed transport or on a role in the regulation of cytoskeletal organization.

Epithelium and endothelium

In an excellent review, Breitkreutz et al. (2009) recalled current knowledge about a highly specialized form of the ECM, the basement membrane (BM). By focusing on BMs in skin and micro-vasculature, the authors gave detailed information about molecular components of these structures, which as the main components include members of the laminin protein family, type IV collagen, nidogen and the proteoglycan perlecan. They further focused on nidogen and perlecan, which do not form polymers but are integrated by their multiple binding sites into the laminin/collagen IV scaffold. Genetic experiments and experimental skin models showed that perlecan and nidogen exert different functions, but these vary drastically between tissues and also on the skin types which were used. Possible explanations of these varying functions were discussed, which may include differences in mechanical properties, the molecular composition of the BM or the adjacent ECM. The authors therefore cautioned to use black or white answers for the function of nidogen and perlecan. A detailed investigation on the ECM proteins Fras1/Frem in epithelial BMs of newborn and adult mice has been provided by Pavlakis et al. (2008). Mutations in the human counterparts FRAS1 and FREM2 have been detected in patients suffering from Fraser syndrome (Short et al. 2007). Fraser syndrome is an autosomal recessive congenital disorder characterized by various developmental defects. In their work, the authors focused on the characterization of the localization pattern of the aforementioned proteins by ICC. Frem3 mostly colocalized with collagen VII and was present in a broad range of epithelial BMs, where Fras1, Frem1 and Frem2 were missing. Fras1 and Frem2 were colocalized with Frem3 in the BM of certain skin parts, whereas Frem1 was detected only in the BM of the tail. The authors' findings are in agreement with the hypothesis that Fras1, Frem1 and Frem2 form an interdependent macromolecular protein complex, which is stabilized by the simultaneous interaction of all the three proteins.

The oral mucosa is a stratified squamous epithelium that rapidly renews itself in adult mammals. Hosoya et al. (2008) studied basal keratinocyte migration during re-epithelialization in oral mucosa to gain insights into the role of epithelial stem cells during this process. In embryonic mice, the authors administered BrdU to mark basal keratinocytes and generated epithelial defects via laser irradiation on the buccal mucosa 2 weeks after BrdU application. In the unwounded epithelium, cytokeratin 14, p63, and BrdU were localized within the basal layer of the epithelium, but the majority of cells within the regenerated epithelium were immunopositive for these proteins. Also, after laser irradiation, basal keratinocytes facing the tips of the papillae evidenced positive immunoreactivity for PCNA, a stem cell marker, and BrdU. This led the authors to speculate that these epithelial stem cells might migrate laterally with other basal keratinocytes to promote skin repair after lesions. Transient receptor potential channel vanilloid (TRPV) proteins are known to also function as thermosensitive receptors (Benham et al. 2003). TRPV2, for example, is known to be activated by high temperatures above 52°C. By using IHC and immuno-EM, Shimohira et al. (2009) provided conclusive data on TRPV2 expression in rat oral mucosa, as this epithelium is known to confer protection against physical, chemical and thermal stimuli. TRPV2 was found to be highly expressed in junctional epithelial cells, little in Langerhans and dendritic cells but not in oral sulcular

epithelial cells or oral epithelial cells. TRPV2 localization on the plasma membrane of unmyelinated and thinly myelinated axons and in venule endothelial cells was also detected. The authors concluded from their findings that TRPV2 might indeed function as a thermosensitive receptor, which is properly localized to perceive environmental stimuli.

A series of recent articles focused on the role of small GTPases in endothelial cells (Baumer et al. 2008a, b; Wang et al. 2008a). In a comprehensive study, Baumer et al. (2008a) investigated the roles of small GTPases RhoA, Rac1 and Cdc42 in endothelial cells of different origins. By using microvascular endothelial cells from dermal, mesenteric or myocardial origin as well as macrovascular pulmonary endothelial cells, differences in the function of small Rho GTPases have been found. As an important outcome, the authors noted that the requirement of Rac1 for endothelial barrier maintenance seemed to be important for all endothelial cells, the barrier-destabilizing role of RhoA, however, was clearly dependent on the endothelial background. The same group further investigated the protective role of Rac1 by focusing on endothelial barrier stabilization via cAMP (Baumer et al. 2008b). cAMP is known to stabilize endothelial barrier functions by regulation of the cadherin of the endothelium, VE-cadherin (Fukuhara et al. 2005). In human dermal microvascular endothelial cells (HDMEC), pharmacological treatment to increase cAMP clearly enhanced endothelial barrier properties, which was also paralleled by activation of Rac1 but not RhoA. Thrombin, as a physiological mediator of inflammation, decreased the endothelial barrier and inactivated Rac1, which was, however, blocked by concomitant pharmacological increase of cAMP. Based on these findings, the authors argued that Rac1 activation likely contributes to the barrier-stabilizing effects of cAMP in microvascular endothelium. Wang et al. (2008a) also studied endothelial cells, but shifted their focus on integrin-mediated signaling. The authors showed that sphingosine-1-phosphate (S1P), a bioactive lipid mediator for various endothelial processes including proliferation, adhesion and chemotaxis (Kim et al. 2009c), activated integrin $\alpha v\beta 3$ in lamellipodia of endothelial cells via the S1P receptor subtype 1, which in another study of the group had been shown to shuttle to the nucleus (Estrada et al. 2009). S1P further induced association of focal adhesion kinase and cytoskeletal proteins with integrin $\alpha v\beta 3$ and promoted enhanced endothelial migration on vitronectin-coated substrata. In experiments using S1P receptor subtype 1 siRNA or dominant-negative-Rho family GTPases, these effects were abrogated, leading the authors to hypothesize that activation of integrin $\alpha v\beta 3$ via S1P- and Rho GTPase-mediated signaling is important for S1P-stimulated chemotactic responses of endothelial cells.

Kredy-Farhan et al. (2008) studied the localization of cortactin in cell–cell contacts of cultured bovine corneal endothelial cells. Cortactin is a phosphotyrosine protein and expressed as two known isoforms, p80 and p85 (Cosen-Binker and Kapus 2006). Cortactin is further known to localize at cell–cell contacts separate from the cortical actin ring, which was confirmed in bovine corneal endothelial cells. In biochemical experiments, the authors found that the isoform p80 was phosphorylated at tyrosin 421 and associated with the triton-insoluble fraction, whereas the isoform p85 was phosphorylated at tyrosin 466 and associated with the triton-insoluble fraction indicating different roles and preferential localizations and associations of these two isoforms.

Toth et al. (2008) aimed at clarifying the receptor profile of the female sex hormones estradiol and progesterone in human umbilical vascular endothelial cells. Both receptors are members of the steroid hormone superfamily of ligand-dependent transcription factors. Extending prior studies which lacked the knowledge of the full repertoire of these receptor families, the authors applied ICC and quantitative RT-PCR to show that these cells express ERβ and progesterone receptor A but not the other variant ERα and progesterone receptor B.

Organs and systems

Skin

In skin, urea plays an important moisturizing role and helps maintaining the epidermal barrier function (Swanbeck 1992). L-Arginine is metabolized by two pathways: by nitric oxide synthase to L-citrulline and nitric oxide and secondly by arginase forming L-ornithine and urea. The balance of these pathways is often disturbed in pathological conditions, including psoriasis. Jaeger et al. (2008) studied the localization of cationic amino acid transporters (hCATs) 1 and 2 in human skin, because these are known to transport L-arginine into keratinocytes. Immunohistochemical comparison between healthy and psoriatic skin revealed a decreased amount of hCAT1, but not hCAT2, in the stratum granulosum of psoriatic skin. In cell culture experiments, the authors, however, were able to show that supraphysiological concentrations of 15 mM L-arginine led to a significant increase of the hCAT1-mRNA and protein expression, but also led to downregulation of the hCAT2B transporter. These findings might open new possibilities using L-arginine as a possible therapeutic agent to reduce psoriatic symptoms.

Ets family transcription factors play important roles during growth and development (Dwyer et al. 2007). The Elf5/ESE-2 transcription factor is a member of the epithelium-specific

Ets subfamily of Ets transcription factors. Choi et al. (2008) recently generated an Elf5-LacZ mouse to study expression of this transcription factor during mouse development. By using this highly sensitive β-galactosidase reporter gene previously undiscovered, expression sites for Elf5 in the differentiated cells of the inner root sheath of hair follicle have been reported.

Vasculature

Embryonic coronary vessel formation has been considered to be a result of both vasculogenesis (de novo formation) and angiogenesis (generation of new vessels from the pre-existing ones by sprouting) (Semenza 2007). Formation of so-called blood-islands containing erythroblasts and endothelial cells normally precedes vasculogenesis. Ratajska et al. (2009) now characterized blood islands in mouse embryonic hearts from 11 dpc through 13 dpc, which is prior to the establishment of the coronary circulation. The authors found two types of blood islands: one formed by migrating nucleated erythroblasts and endothelial cells and the second one by emergence of erythroblast-like and endothelial-cell progenitors. Subepicardial blood islands also contained nucleated erythroblasts, undifferentiated mesenchymal cells, platelets and early lymphocytes. These findings led the authors to speculate that embryonic heart vasculogenesis is accompanied by hematopoiesis in mice. Marini et al. (2008) were interested in myocardial angiogenesis in the rat. Enhanced angiogenesis is important for the beneficial effects of exercise training on the myocardium. The authors examined if 10-week training-induced increases in vascularization persisted also after 4 weeks of detraining. In this group, the left ventricle capillarization and von Willebrand-positive cell densities only partially reversed to untrained control conditions, although markers of angiogenesis such as VEGF and HIF-1α returned to baseline value after detraining. The authors concluded from their findings that training-induced increase in cardiac capillarization is retained for some time upon cessation of the training program even in the absence of angiogenic stimuli.

The lymphatic vasculature is an essential part of the circulatory system and used for drainage of tissue fluid and transport of immune cells and emulsions of fat. A recent review by Maby-El Hajjami and Petrova (2008) highlighted pathologic situations of the lymphatic vascular biology, including lymphedema, inflammatory diseases and tumor metastasis. Similar to blood vessels, development of lymph vessels is controlled by several molecules, including members of vascular endothelial growth factor and angiopoietin families. In an extensive immunohistochemical analysis, Shimoda and co-workers demonstrated angiopoietin-2 (Ang2) in lymphatic vascular development in mice. By comparison with early lymphatic endothelial markers, such as Prox1 or LYVE-1, lymphatic progenitor cells were Ang2-positive at earliest stages of lymphvasculogenesis and thereafter. Also immunoreactivity for Tie2, a primary receptor for angiopoietins, was detected. All these findings indicated that lymphatic endothelial cells might regulate lymphatic development via their own Ang2-Tie2 signaling.

Salivary glands

The duct system of the submandibular gland of rodents is composed of the intercalated duct (ID), striated duct (SD), granular convoluted tubule (GCT) and excretory duct, and also shows a sexual dimorphism, because the granular convoluted tubule is developed preferentially in males during puberty. This can also be mimicked by application of testosterone to female mice. Keattikunpairoj et al. (2009) recently worked on cAMP response element-binding proteins (CREB) in the duct system of mouse submandibular glands to investigate this sexual dimorphism in detail. In Western blotting experiments, both total and phosphorylated CREB were significantly enhanced in the female submandibular glands and localized to the nuclei of intercalated duct cells and a subpopulation of striated duct cells. Castration of male rats led to an increase in CREB, whereas administration of testosterone to females decreased CREB levels. These findings could imply the involvement of CREBs in the androgen-dependent differentiation of the duct system.

Brauer et al. (2009) recently documented the expression and secretion of surfactant proteins A, B, C and D in human parotid and submandibular glands. These proteins may be involved in the immune defense inside the oral cavity which is exposed to pathogenic environmental stimuli. Indeed, RT-PCR analyses demonstrated expression of mRNA for SP-A, -B, -C and -D in both glands of healthy individuals. Moreover, Western blot analysis and IHC confirmed these findings, leading the authors to speculate on the potential function of these proteins inside the oral cavity.

Bingle and Craven (2002) recently dealt with a putative family of host defense proteins in the mouse, which include Palate lung nasal clone (PLUNC) as a founding member. PLUNC is expressed in the upper respiratory tract and oral cavity. In the new study, the authors gave a detailed characterization on SPLUNC2, the human ortholog of the rodent parotid secretory protein (Bingle et al. 2009). By generating novel affinity-purified antibodies to SPLUNC2 and Western blotting experiments, several distinct protein bands in saliva were detected, together with immunoreactivity in serous cells of the major and minor salivary glands. However, antibodies directed against distinct epitopes yielded different staining patterns. RT-PCR and expressed sequence tag analysis finally also confirmed that SPLUNC underwent alternative splicing.

Kidney

AQPs are transmembrane proteins facilitating the transfer of water and small solutes across cellular membranes (Kwon et al. 2009). Extending previous study in MDCK cells (Hasegawa et al. 2007), Takata et al. (2008) lately reviewed the function of a AQPs in water transport in kidney. After summarizing functions and specializations of the various AQP, the authors focused on AQP2, which is especially important, because it is regulated by the anti-diuretic hormone (ADH), and therefore plays an essential role in water reabsorption. The authors gave detailed information about the expression, regulation and also intracellular trafficking of AQP2. Upon ADH stimulation, AQP2 is incorporated into the apical plasma membrane by fusion of pre-existing vesicle. This process is initiated by AQP2 phosphorylation via protein kinase A. The review also addressed secretion of AQP2 in the urine via exosomes and molecular interactions of AQP2 with the cytoskeleton, and rendered it clear for the reader that AQP2 in the kidney not only plays a critical role in maintaining but also modulating water transport.

Uptake and excretion of monocarboxylates (e.g. lactate, pyruvate, and ketone bodies) are crucial processes in the regulation of both energy metabolism and pH (Poole and Halestrap 1993). The renal tubular system utilizes lactate and ketone bodies as the major fuels, since these cells in the renal medulla must function in anaerobic conditions. These cells also excrete glycolytically derived lactate into the blood circulation to avoid cellular acidosis. With their recent work, Yanase and co-workers tried to investigate renal energy metabolism by analyzing the cellular expression of a sodium-dependent monocarboxylate transporter (SMCT) and proton-coupled monocarboxylate transporters (MCT) in the mouse kidney. ISH experiments yielded high signals for SMCT (cortex and outer stripe of the outer medulla), MCT2 and MCT8 (inner stripe of outer medulla and the cortex, respectively). Detailed immunohistochemical images clearly detected SMCT in the brush border of proximal tubules, whereas MCT2 was found basolaterally in thick ascending limbs of Henle's loop. The authors noted that these findings, however, did not support a functional linkage between these two classes of monocarboxylate transporters. In another study of the same group, expression of MCT1 in the mammary and sebaceous gland of mice was reported (Takebe et al. 2009). The study by Kirat and Kato (2009) confirmed the findings of MCT1 in the mammary gland of lactating cows, but also succeeded to detect mRNA and protein for isoforms MCT2, 3, 4, 5 and 8. Both localization of MCT isoforms in the apical and basolateral membrane of the mammary alveolar epithelium was detected by the authors indicating roles in milk synthesis and secretion.

Proteins of the olfactomedin family are named according to their conserved C-terminal olfactomedin domain and have functions in various tissues (Tomarev and Nakaya 2009). Goldwich et al. (2009) lately focused their research on myocilin, a secreted and potentially ECM-adhesive protein of the olfactomedin family which is associated with juvenile forms of glaucoma and also expressed in podocytes. During mesangioproliferative glomerulonephritis, it is also induced in mesangial cells (Goldwich et al. 2005). Coating of cell culture plates with recombinant full-length but not C-terminal fragmented myocilin induced adhesion of a rat podocyte cell line and rat primary mesangial cells. This adhesion, however, was less effective than fibronectin or collagen I, but synergistic effects of myocilin and fibronectin were observed. Also sprouting of cells and formation of focal contacts were seen. The authors' findings imply important functions of myocilin in cell–matrix interactions of the glomerulus.

The armadillo repeat gene deleted in velo cardio facial syndrome (ARVCF) is a member of the p120 subfamily and together with β-catenin and plakoglobin belongs to the family of arm-repeat proteins. Immunohistochemical localization of these proteins has been hindered by lack of availability of appropriate antibodies. Walter et al. (2008), however, generated novel mono- and polyclonal antibodies targeted against ARVCF. Among the tissues studied by the authors, ARVCF displayed prominent localization in nephron segments of human and mouse kidney. In co-immunostaining experiments, ARVCF was shown to localize in proximal tubules. Besides, it was also detected in early stages of mouse development. Although it is known to regulate cell adhesion, ARVCF was detected in only one kidney cell line at cell membranes but mostly inside the cytoplasm as granular vesicles. This work highlighted the potential role of ARVCF in the proximal tubules of kidney.

In a study with interesting implications, using the technique of 5′-rapid amplification of cDNA ends, Hentschke et al. (2009) found alternative transcriptional starts sites coding for N-terminal protein variants of the anion exchanger AE4. AE4 is known to be primarily expressed in the collecting duct of kidney. The authors further found a 5′ genomic region with high transcriptional activity among various species. They also generated transgenic mice with β-galactosidase expression driven by this fragment. Marker activity was seen in type B intercalated cells, similar to endogenous AE4 expression. In light of these findings, this sequence could be used as a type B intercalated cells-specific promoter in future genetic studies.

Gubhaju et al. (2008) used the baboon monkey as an animal model to investigate stem cell markers in the developing baboon kidney. They focused on TRA-1-60, TRA-1-81 and GCTM-2, which all recognize specific epitopes formed by modification of a common keratan sulfate core molecule.

Podocalyxin was used as marker for hematopoietic progenitor cells. The authors found that in kidneys with on-going nephrogenesis all markers except podocalyxin were specifically localized to the apical plasma membrane of the epithelium of the ureteric ampullae and the collecting ducts. In kidneys with completed nephrogenesis, the localization of the markers was limited to the collecting ducts. Further experiments need to determine the identity of the cells identified by these stem cell markers.

The urothelium is a multi-layered epithelium covering the luminal side of the urinary bladder and urether. During regeneration of the urothelium, superficial cell desquamation is followed by differentiation of newly exposed superficial cells. Veranic et al. (2009) identified chitosan, a widely used food additive with lipid binding abilities, as a potent inducer of urothelial cell desquamation. In vivo experiments in mice found that intraluminal chitosan treatment led to rapid (20 min) removal of the superficial cell layer of the bladder. The authors also studied differentiation of the newly formed superficial layers by using the markers ZO1 and cytokeratin 20. As potential clinical application of chitosan, the authors mentioned chronic cystitis caused by *Escherichia coli* hiding in superficial umbrella cells (Mulvey et al. 1998). Specific ablation of these cells by chitosan may be a promising way to clear the majority of bacteria from the bladder.

Intestine

The intestinal mucosa acts as a cellular barrier between the gut and the intestinal lumen, thereby controlling the passage of ions, molecules and microorganisms. Organotypical cell cultures are important models for analyzing cellular interactions of the mucosal epithelium and pathogenic mechanisms in the gastrointestinal tract. A recent study by Bareiss et al. (2008) described a novel three-dimensional organotypical tissue culture from adult murine colon. Explants could be cultured for up to 2 weeks under these conditions and maintained typical characteristics of the intestinal mucosa. Physiological function of the system was tested by application of dexamethasone that resulted in a strong upregulation of the serum- and glucocorticoid-inducible kinase 1 which is also found in vivo. Moreover, pathogenic situations were tested by coculture with different *Candida albicans* strains. The results make this approach a promising tool to easily investigate cell biological phenomena in the intestine.

Interstitial cells of Cajal play an important role in the regulation of gastrointestinal motility (Thomsen et al. 1998). These cells express the c-Kit, a tyrosine kinase receptor (Huizinga et al. 1995), which is essential for survival and proliferation of cells during embryonic and neonatal periods. Mei et al. (2009) evaluated c-Kit-positive interstitial cells of Cajal situated around myenteric nerve plexus in 0–56-day-old murine small intestine. The density of myenteric interstitial cells of Cajal increased from P0 to P12, but decreased until P32. However, the total amount increased more than 15-fold up to P32. With the help of BrdU pulse chaise experiments, the authors' findings indicated that an age-dependent proliferation is involved in the postnatal development of interstitial cells of Cajal, resulting in greatly increased cell numbers probably originating from progenitor cells. Platelet-derived growth factor receptors (PDGFRs) belong to the same kinase group as c-Kit expressed by interstitial cells of Cajal. Iino et al. (2009) consequently addressed the question whether PDGFRα-positive cells reside in the gastrointestinal tract. PDGFRα-immunopositive cells, which were observed in the musculature throughout gastrointestinal tract, were distinct from interstitial cells of Cajal and neurons but closely associated with enteric nerve fibers. The distribution of these cells in mice lacking interstitial cells of Cajal was unaltered though. Some of these cells also were immunopositive for the SK3 potassium channel and consequently were considered fibroblast-like cells or non-Cajal interstitial cells.

The functional renewal unit of the small intestine, the crypt–villus axis, makes it an attractive model to study epithelial cell proliferation and maturation. Dydensborg et al. (2009) presented a detailed study on the differential expression of the integrins α6Aβ4 and α6Bβ4 along the crypt-villus axis in the human small intestine in order to correlate the localization with different stages of proliferation or differentiation. These two integrin variants have been shown to exhibit potentially distinct biochemical properties. Immunocytochemical images clearly identified the α6A variant in proliferative cells of the crypt, whereas differentiated enterocytes and Paneth cells expressed the α6B variant. This was also confirmed in RT-PCR experiments using the Caco-2 cell culture model. Overexpression studies demonstrated that α6A manipulated transcriptional activities related to cell proliferation, leading the authors to suggest that this subunit indeed is involved in the intestinal epithelial cell renewal process.

The lipopolysaccharide (LPS)-binding protein (LBP) is a known acute-phase protein and belongs to the family of other lipid transfer/lipopolysaccharide-binding proteins, including the cholesteryl ester transfer protein and the bacteriocidal permeability increasing protein (Schumann et al. 1990). Inspired by the expression of LBP by Caco-2 cells, Hansen et al. (2009) performed a detailed analysis of LBP localization in the mouse small intestine. Interestingly, an antibody against LBP distinctly labeled a small population of cells located at the bottom of crypts. These cells were identified as Paneth cells because of positivity for lysozyme and α-defensin 4. Ultrastructurally, intense labeling in the secretory granules of these cells was observed. Based on

these findings, LBS may function in the innate immune response of the gut.

The small intestine has a key function in the absorption of dietary nutrients, including fatty acids. Cytosolic fatty acid binding proteins (FABP) are thought to permit the binding and transport of mainly fatty acids through the cytosol to cell organelles (Ono 2005). The localization and function of two FABP forms (I- and L-FABP) was addressed in a study by Levy et al. (2009). Immunofluorescence staining of L-FABP was barely detectable in the lower half of the villus and the crypts, whereas I-FABP was visualized in epithelial cells of the entire crypt-villus axis in all intestinal segments. Immunogold experiments revealed more intense but heterogenous labeling of L-FABP compared with I-FABP, accompanied with a heterogeneous distribution in the cytoplasm, microvilli and basolateral membranes. Western blot experiments predominantly localized both isoforms in jejunum. Transfection of Caco-2 cells with I-FABP cDNA resulted in decreased lipid export, apolipoprotein biogenesis and chylomicron secretion. Localization of the epidermal type FABP (E-FABP) in most of the dendritic cells of the subepithelial domes, follicles of Peyer's plaques and M cells in the follicle-associated epithelium of mouse intestine was reported lately by Suzuki et al. (2009a).

Liver

The liver is important not only for the storage and release of nutrients but also for the neutralization and elimination of a variety of toxic substances. These functions are bound to distinct cellular constituents and compartments. In a meticulous study, Baratta et al. (2009) characterized the cellular organization of the normal mouse liver. The authors used LM, EM and quantitative immunocytochemical techniques. General histological organization was similar to other species. By using specific markers, including intravascularly administered latex microspheres, the authors stated that 52% of all labeled cells represented hepatocytes (many of these were multinucleated), 18% Kupffer cells, 8% Ito and 22% endothelial cells. The close similarity to other mammalian species again proposed the mouse as a useful animal model for studies of liver structure and function.

Mansuroglu et al. (2009) questioned whether passaged rat fetal liver cells were functional hepatoblasts. Therefore, the authors compared hepatoblast and liver myofibroblast gene expressions of adult and fetal rat liver tissues with primary and passaged cultures of isolated rat fetal liver cells. Markers such as desmin and α-smooth muscle actin as well as Prox1 or α-fetoprotein have been used. As a main outcome it was concluded that myofibroblasts became the major cell population of fetal liver cell cultures during passages. The authors cautioned that this observation needs to be taken into account when passaged fetal liver cells are used for transplantation.

In another study, the same group focused on fibroblastic cell types of the liver (Dudas et al. 2009). Several fibroblastic cell types were characterized, including hepatic stellate cells, transitional cells, and myofibroblasts. In their article, the authors assessed expression of the fibroblast adhesion molecule Thy-1 (CD90) in liver fibroblast populations in the context of acute or chronic liver injury. In vivo animal models as well as isolated human liver myofibroblasts were used to demonstrate that Thy-1 is a functional marker of liver (myo)fibroblasts but not of hepatic stellate cells in normal, injured and regenerating rat liver, and is located to zone 1 of the liver lobule. Better markers for quiescent and activated hepatic stellate cells were described by Van Rossen et al. (2009). In FFPE samples, normal and diseased human livers were studied. After testing various markers, cellular retinol-binding protein-1 and vinculin were found to selectively stain hepatic stellate cells in human liver tissues.

The mammalian liver is unique in its capability to regenerate after injury or hepatectomy by proliferation of liver progenitor cells, so-called oval cells. Chiu et al. (2009) used a 2-acetylaminofluorene/carbon tetrachloride rat liver injury model to study the gene profile of hepatic cells under proliferating conditions. In their microarray analysis, the authors focused on adhesion molecules, ECM proteins, MMPs, growth factors and cytokines. Among the strongly upregulated genes, MMP-7 and CD44 results were verified by immunostaining to correspond to oval cells. Moreover, newly differentiated cytokeratin-19-positive hepatocytes within foci did not show CD44 staining, which led the authors to suggest that CD44 is related to the undifferentiated oval-cell phenotype. In CD44-deficient mice fed with an oval cell-inducing diet significantly reduced oval cell reactivity was found. These results suggested that CD44 might play critical roles in the proliferation and differentiation of hepatic oval cells. A recent study also provided a novel protocol for the enrichment of hepatic progenitor cells from human fetal liver by transfection of a vector coding for EGFP under the α-fetoprotein promoter and subsequent fluorescence-activated cell sorting (Wang et al. 2008b).

Endocrine system

Atrial (ANP), brain (BNP) and C-type natriuretic peptide (CNP) are members of a family of natriuretic peptides important for cardiovascular homeostasis (Rosenzweig and Seidman 1991). ANP and BNP are produced and released mainly from atrial and ventricular cardiomyocytes. The effects of these peptides are mediated by three natriuretic peptide receptor subtypes, NPR-A (ANP, BNP), NPR-B

(CNP) and NPR-C (ANP, BNP, CNP). After previous reports of expression of ANP and a potential receptor in the pancreas, Burgess et al. (2009) aimed at identifying the ANP receptor subtype in the human pancreas. NPR-C immunoreactivity, but neither ANP nor NPR-A, was detected in human islets. NPR-C was localized mainly in glucagon-containing α cells. In functional experiments, all three natriuretic peptides and a pharmacological agonist of NPR-C stimulated glucagon secretion from perfused human islets, providing compelling evidence for a role of natriuretic peptides in the regulation of glucagon secretion.

Octamer-binding transcription factor-4 (Oct4) is a nuclear transcription factor that is involved in the generation of induced pluripotent stem cells (Takahashi et al. 2007). Oct4 is a key regulator of pluripotency in the early mammalian embryo. Wang et al. (2009) recently provided evidence that Oct4 is expressed in nestin-positive cells as a novel marker for pancreatic endocrine progenitors. The authors' findings were confirmed by RT-PCR, Western blot and IHC assays. In double staining experiments, colocalization of Oct4 together with the endocrine peptide chromogranin A and Ngn3, the transcription factor for pancreatic endocrine precursors, was detected, indicating that Oct4 can be used as novel and suitable marker for pancreatic development.

By applying the signal sequence trap method (Tashiro et al. 1999) to a cDNA library of embryonic rat pituitary, Nakakura et al. (2009) revealed the abundant expression of delta-like protein 1 (Dlk1) in this gland. Dlk1 is an epidermal growth factor-like repeat protein maintaining the preadipose state in preadipocytes (Nueda et al. 2007). The finding of the first screen was validated with ISH. Immunocytochemical staining first detected the protein in the Rathke's pouch and the infundibulum, with later restriction to the pars distalis and pars tuberalis. Further experiments are needed to clarify the exact role of Dlk1 in pituary development.

Male reproductive system

Prominins show a typical pentaspan membrane topology, but the function of these cholesterol-binding proteins in embryonic and adult epithelial cells is still unclear (Corbeil et al. 2001). Jaszai et al. (2008) characterized expression of prominin-1 and 2 along the adult male reproductive system and urinary bladder in male mice by ISH experiments. In contrast to tissues derived from epigonadal mesonephric tubules (i.e. ductuli efferentes) or from the Wolffian tube (e.g. corpus epididymidis and vesicula seminalis), the urinary bladder epithelium which derives from the sinus urogenitalis expressed exclusively prominin-2 but not prominin-1. The testis was found to expresses only prominin-1, but not prominin-2.

Kim et al. (2009b) recently focused on CREB in mouse testis during development and spermatogenesis. CREB activity was significantly higher in early phase developing testis than in adult testis, and changes in CREB phosphorylation status have been observed. Phosphorylation in seminiferous tubules of the adult testis varied according to the spermatogenic cycle. Intense phosphorylation signals were detected in spermatogonia of all stages and in elongating spermatids, which led the authors to speculate on potential roles of CREB for spermatogenesis in mouse testis.

The blood-testis barrier is built up by parallel-arrayed TJs on basally located lateral processes of Sertoli cells. Fink et al. (2009) reported that claudin-11 is overexpressed and mislocated from the blood-testis barrier in Sertoli cells of testicular intraepithelial neoplasia, which led the authors to speculate that a dysfunction of claudin-11 rather than a failure of expression leads to disruption of the blood-testis barrier in testicular intraepithelial neoplasia. Another study by Ruttinger et al. (2008) investigated the expression of Cx43 in the context of testicular neoplasia of the dog. In canine testicular tumors Cx43 mRNA was detectable in both seminoma and neoplastic Sertoli cells, but Cx43 at the protein level was found only in neoplastic Sertoli cells.

In their recent study, Tsikolia et al. (2009) described a novel marker for fetal Leydig precursor cells, c-Kit. c-Kit IHC clearly displayed a gender specific expression variation in gonads. c-Kit expression was continuous in interstitial cells of male fetuses, which were identified as Leydig cells by double staining with cytochrome P450 side chain cleavage enzyme and steroidogenic acute regulatory protein. Isolation of c-Kit-positive cells retained their steroidogenic capacity in vitro, providing a useful strategy to purify fetal Leydig cells for advanced studies. For polyamine synthesis, ornithine decarboxylase (ODC) is an essential enzyme, and therefore linked to cell proliferation and differentiation (Pegg 2006). High ODC activity is associated with rapidly proliferating normal and malignant cells. In steroidogenic cells of human gonads, Makitie et al. (2009) found high expression of antizyme inhibitor 2, an activator of ODC. ISH and ICC studies identified high expression of antizyme inhibitor 2 not only in normal Leydig cells and Leydig cell tumors but also in ovarian luteinized cells and in hilum cells implying a possible involvement in the release of steroid hormones.

In mammalian spermatozoa, Ca^{2+} signals are considered as prime regulators of sperm motility and fertilization capacity (Publicover et al. 2008). Efficient Ca^{2+} homeostasis must include processes to remove Ca^{2+} ions from the spermatid cytosol. This is either performed by the Na^{+}/Ca^{2+} exchanger, the plasma membrane Ca^{2+}-ATPase (PMCA) or SERCAs. Wilhelm et al. (2008) lately demonstrated that PMCA4 is conserved in sperm from testis to epididymis. In testis, PMCA4 protein was detected in spermatogonia, late

spermatocytes, spermatids and in epididymal sperm. In epididymis, PMCA4 protein was detectable only in the epithelial cells of the caput in contrast to PMCA4 mRNA. Furthermore, an identical distribution of the two PMCA4 splice variants was detected and only in the caput epididymidis; variant 4b was more prominent.

Endostatin is known to be processed from collagen 18 and acts as an inhibitor of angiogenesis and as a potential anti-tumorigenic protein (Fu et al. 2009). Recent ISH and IHC experiments by Tilki et al. (2008) revealed high levels of the collagen 18 and endostatin in rete testis and epididymis. The authors speculated that this finding might, at least in part, explain why rete testis and epididymis are rare locations for primary tumors or metastasis.

Postnatal morphogenesis of the rat ventral prostate has been the topic of a recent study by Bruni-Cardoso et al. (2008). Because the initial events in prostatic morphogenesis include cell proliferation, epithelial canalization and outgrowth toward the stroma, the authors hypothesized that MMP-2 and MMP-9 may be involved in these stromal rearrangements. Activities of MMP-2 and MMP-9 were detected, but MMP-2/MMP-9 expression decreased during the first week. Epithelial cords showed strong and diffuse gelatinolytic activity, which was paralleled with distribution of MMP-2. MMP-9, however, was rather concentrated at epithelial tips. Although functional studies were lacking, these findings provided first hints for a contribution of MMP for prostatic remodeling.

The activation of purinoceptors is influenced by surface ectonucleotidases that modulate the concentration of extracellular nucleotides (Zimmermann 2006). Among these, the ectonucleoside triphosphate diphosphohydrolase (E-NTPDase) family with its four plasma membrane bound members, NTPDase1, NTPDase2, NTPDase3 and NTPDase8, constitutes the most abundant one. Martin-Satue et al. (2009) investigated these NTPDases in the murine reproductive tract because extracellular nucleotides such as ATP have been shown to influence various processes, for example spermatogenesis. Interestingly, NTPDase1 was detected in Sertoli cells as well as in ovarian granulosa cells. NTPDase2 was largely expressed by cells in the connective tissue, NTPDase3 in secretory epithelia, but NTPDase8 remained undetected.

Female reproductive system

Somatostatin is a peptide hormone that is secreted from the hypothalamus into the portal circulation to inhibit growth hormone secretion in the anterior pituitary (Moller et al. 2003). Effects of multiple somatostatin administration on the pituitary-ovarian axis in female rats were presented by Nestorovic et al. (2008) in a recent article. Somatostatin application resulted in diminished cell volumes of FSH, LH and GH-immunoreactive cells, whereas the total number of these cells was unchanged. This was accompanied with a decrease of FSH and LH in serum and an increase in the number of primordial but the absence of preovulatory follicles in ovaries. The authors proposed that somatostatin markedly inhibited pituitary FSH, LH and GH cells and inhibited folliculogenesis in ovaries.

Lohr et al. (2008) succeeded in providing conclusive data on the cell type-specific expression of galectin-3, compared to homodimeric galectins-1 and -7. Galectin-3 is known as a multifunctional protein with modular design (Dumic et al. 2006). In murine ovaries, galectin 1 and 7 were confined to the surface epithelium, whereas galectin-3 was found in macrophages of the cortical interstitium between developing follicles and medullary interstitium. Moreover, strong signals were detected in granulosa cells of atretic preantral follicles, and increasing positivity was seen in corpora lutea upon regression.

Estrogens play an important role in female reproduction, with the ovary serving as both the primary site of estrogen synthesis and a major estrogen target. Using cultured mouse ovarian follicles, Lenie and Smitz (2008) gave a detailed characterization of the ER subtype shift in ovarian follicles in culture. Physiologically, the receptor variant ERβ is mostly expressed in granulosa cells and ERα in theca cells. In cultured cells, ERβ was found exclusively in granulosa cell nuclei regardless of growth stage or culture conditions, whereas ERα localized to oocytes, granulosa and theca cells and displayed changing localizations between growth stages and culture conditions. Strikingly, hCG application led to strongly reduced ERβ protein levels in luteinized granulosa cells, while ERα immunostainings shifted to cytoplasmic regions in all but theca cells. The authors finally concluded that both ERα and ERβ are present within granulosa cells of cultured follicles, but display a different subcellular localization during in vitro preantral follicular development. Adding to this, Xu et al. (2009a) provided interesting data on the expression of a novel variant of ERα, ERα36. In immunostainings, ERα36 was consistently detected in nuclei of oocytes, but immunosignals were smeared in granulosa cells. However, the ER-α36 signal was upregulated in the cytoplasm but not nuclei of the developing corpus luteum. With experiments using a function-blocking antibody, the author provided further evidence for an important role of this ERα variant in oocyte development.

Tubal pregnancy is unique in women because in other mammals it occurs neither spontaneously nor experimentally (Corpa 2006). For this reason, Makrigiannakis et al. (2009) characterized the expression of receptivity markers in the fallopian tube epithelium. These include pinopodes as morphological markers studied by EM and integrins $\alpha v\beta 3$, $\alpha v\beta 5$ and their ligands as the molecular markers.

Surprisingly, in the tubal epithelium pinopodes were detected exclusively during day LH +7, coincident with their formation in the endometrium and increase of integrin $\alpha v\beta 3$ in oviduct epithelium.

Steffl et al. (2009) focused on growth hormone receptor (GH-R) in the oviduct of pregnant pigs. During all stages of the estrus cycle and pregnancy, GH-R mRNA and protein were found in the porcine oviduct. Localization of GH-R was mainly observed in the cytoplasm of ciliated epithelial cells. Additionally, GH-R mRNA was detected in porcine conceptuses collected at day 18 of pregnancy concomitant with exclusive GH-R immunostainings of the trophectoderm. These novel findings might indicate new functions of auto- or paracrine GH signaling in the porcine oviduct or pig trophectoderm.

Soon after the primordial germ cells reach the genital ridge, the mammalian oocyte enters meiosis and becomes arrested at the prophase of the first meiotic division (Mehlmann 2005). Upon follicular recruitment, the oocyte enters the growth phase and after completing the growth phase the oocyte becomes transcriptionally inactive (Mehlmann 2005). Fulka et al. (2009) used an oocyte fusion model to determine if the fully grown germinal vesicle stage oocyte could induce suppression of transcription activity in transcribing germinal vesicle stage oocytes. Although the authors identified mechanisms for silencing transcription, such as RNA polymerase II degradation and rearrangement of splicing proteins in mature oocytes, these oocytes were insufficient to induce these changes in transcriptionally active nuclei, which led the authors to discuss the selection of cytoplasts in nuclear transfer experiments.

Proper invasion of the trophoblast into the endometrium is crucial for normal placentation. Zhang et al. (2009) examined the protein phosphatase 1A (PPM1A) during human cytotrophoblast cell invasion and migration. This phosphatase is involved in the inactivation of a broad range of substrates, including transforming growth factor (TGF)-β, MAP, p38 and JNK kinases. High PPM1A expression of placental villi at term as compared with that during the first trimester was detected. In experiments using an extravillous trophoblast cell line, knockdown of PPM1A promoted both motility and invasiveness by upregulation of MMPs.

Adipokine hormones affect not only metabolism and obesity but also fertility and female reproduction (Wiecek et al. 2007). The expression of adipokines during preimplantation of rabbit and mice embryos was the topic of a recent study by Schmidt et al. (2008). The adipokine adiponectin as well as its receptors were localized in glandular endometrial epithelium several days p.c.. Moreover, both trophoblast and embryoblast were positive for adiponectin, but a specific switch in its receptor expression was detected linking to a role of the adipokine network in blastocyst differentiation.

During early pregnancy in the rat, focal adhesions in uterine luminal epithelial cells collapse to facilitate invasion of the implanting blastocyst into endometrial decidual cells. Kaneko et al. (2009) recently assessed the effect of ovarian hormones on distribution and protein expression of focal adhesion proteins talin and paxillin in rat uterine luminal and glandular epithelial cells. Progesterone alone or in combination with estrogens, which are also observed at the time of implantation, resulted in reduced concentration of talin and paxillin at the basal cell surface of uterine luminal epithelial but not in uterine glandular epithelial cells. This led the authors to speculate that ovarian hormones differentially regulate focal adhesions in the rat uterus.

Immune system and inflammation

Two recent review articles impressively summarized in vivo visualization of immune cells. While Roediger et al. (2008) focused on imaging dendritic cell migration within the skin, its molecular determinants and appropriate techniques such as skin-fold chambers and multiphoton microscopy, Nitschke et al. (2008) gave a personal but enlightening overview of interesting findings of the first 6 years of intravital multiphoton microscopy in the context of not only immunological questions but also technical progress. This review gives fascinating insights into the dynamic of immunological processes in vivo.

Clusterin, also known as apolipoprotein J, is present in numerous fluids, such as milk, cerebrospinal fluid, blood plasma, and urine, where it may function as an extracellular chaperone (Jones and Jomary 2002). Recently, Verbrugghe et al. (2008) also detected clusterin in M cells and follicular dendritic cells of human gut-associated lymphoid tissue and in germinal centers as well as the lymphoepithelium of tonsils of the Waldeyer's ring. With their study, the authors proposed clusterin as a novel M cell marker, and noted the important role for clusterin in innate immunity.

Mast cells are localized throughout the human body and are involved in immune as well as in allergic reactions. Taildeman et al. (2009) lately characterized mast cells for the expression of leptin and its receptors. Leptin is a cytokine regulating metabolic and immune processes, and is known to be expressed on other immune cells (Maya-Monteiro and Bozza 2008). Both coexpression with mast cell markers chymase or tryptase was found for leptin in human skin which led the authors to speculate on potential immunomodulatory effects of leptin in mast cells.

T lymphocytes developed in the thymus have to be tolerant to self tissue-specific antigens, which is achieved by negative selection of thymocytes during migration in the thymic medulla (Hollander and Peterson 2009). In this process, thymic metallophilic macrophages play an important

role. Milicevic et al. (2009) now presented data that the development of these macrophages is not dependent on the autoimmune regulator (Aire). This finding was concluded by investigating the thymus of Aire-deficient mice, where these cells are fully developed, compared to mice deficient in nuclear factor-κB-inducing kinase (NIK) which acted as negative control animals. The authors interpreted their findings to support an even more important role of lymphotoxin-β receptor signaling for the development of metallophilic macrophages, which had been reported previously (Milicevic et al. 2006). Mikkelsen et al. (2008) put particular emphasis on studying the macrophage system in the intestinal muscularis externa during inflammation. Wildtype and osteopetrotic mice, which lack macrophages in the muscularis externa due to deficiency in colony stimulating factor 1, were challenged with LPS to induce inflammation. In wildtype mice the density of MHCII-positive cells temporarily increased in contrast to F4/80-positive cells, which might represent mononuclear phagocytes, eosinophils and a subset of dendritic cells. Osteopetrotic mice lacked MHCII and F4/80-positive cells after LPS treatment which indicate that these cells are CSF-1-dependent. In both genotypes, LPS induced VCAM-1 activation of vessels and a modest influx of granulocytes.

Novel roles of osteoblasts in human innate immunity have been demonstrated by Varoga et al. (2009). These cells have been found to produce β defensin-3 (HBD-3), an antimicrobial peptide directly targeting microorganisms (Batoni et al. 2006). The authors used samples of both healthy and osteomyelitic human bone as well as primary and immortalized osteoblasts and exposed them to *Staphylococcus aureus* supernatant. HBD-3 was released within hours of bacterial exposure in cultured osteoblasts but not in samples of chronically infected bone. Further experiments indicated that the rapid HBD-3 release was not dependent on de-novo protein synthesis or glucocorticoide involvement but on toll-like-receptors-2 and -4. This led the authors to argue that HBD-3 in osteoblasts is most likely a result of a rapid secretion of preformed HBD-3.

In two excellent recent reviews, Robinson (2008, 2009) summarized recent knowledge of phagocytic leukocytes and ROS. Phagocytic leukocytes, when appropriately stimulated, consume oxygen and produce superoxide and other ROS via the NADPH-oxidase system, a process often referred to as the respiratory burst. The authors gave not only a detailed account on recent insights into the molecular components and interactions of the NADPH-oxidase system, but also important results from microscopic imaging in complementation to biochemical studies were highlighted.

Le Bitoux and Stamenkovic (2008) lately reviewed the role of inflammation during tumor–host interactions. After giving a brief but molecularly detailed overview on inflammation, this review focused on recruitment of leukocytes by tumors, roles of macrophages and lymphocytes in tumor growth and inflammatory mediators in the tumor microenvironment. A chapter not only on chronic inflammation as a possible predisposition to cancer but also on anti-tumor processes of inflammation was provided. Finally, the authors cautioned that the important question whether in the absence of exogenous carcinogens (chronic) inflammation itself could lead to transformation is still unanswered yet.

Central nervous system

The cerebellar cortex is built by granule cells, Purkinje cells and certain types of inhibitory interneurons (Voogd and Glickstein 1998). In a recent review, Schilling et al. (2008) put special emphasis on the interneurons of the cerebellar cortex. Recent research has highlighted the fact that these cells are quite more diverse and heterogeneous than generally appreciated. The authors provided a detailed overview on cerebellar cortical interneuron diversity (basket-, stellate- and Golgi cells, candelabrum neurons, Lugaro cells and unipolar brush cells), and summarized recent results on the development and function of these cells in cerebellar neurobiology.

Olfactory sensory neurons (OSN) are the only neurons situated in a surface epithelium, the olfactory epithelium (OE), and thus participate in establishing an epithelial barrier (Morrison and Costanzo 1992). In a meticulous work, Steinke et al. (2008) outlined the molecular composition of TJ and AJ in the rat OE. The authors used antibodies against TJ proteins occludin, claudins 1-5 and ZO 1-3, as well as AJ proteins N-cadherin, E-cadherin and α-, β- and p120-catenin, and provided a detailed set of images describing the molecular composition of TJs and AJs formed by neuronal, epithelial and glial cells in the OE and fila olfactoria.

Members of the classical transient receptor potential (TRPC) protein family are highly expressed in the central nervous system, and may play important roles in neural stem cell proliferation and central nervous system development (Talavera et al. 2008). Therefore, Boisseau et al. (2009) presented a detailed analysis of TRPC distribution in the embryonic cortex of mice. The mRNAs of all known TRPCs (TRPC1–TRPC7) could be found in the cortex at E13. IHC pointed to a heterogeneous expression of the main TRPC variants 1 (found in post-mitotic neurons of the preplate), 3 (found in non-neural and proliferating cells) and 6 (detected in neuronal and in dividing non-neuronal cells). Moreover, double immunostaining experiments revealed colocalization of TRPC3 together with TRPC6 in a specific subset of cells.

The insula is a lobe of the telencephalon buried in the depth of the lateral fissure. Wai et al. (2008) investigated

human insular cortex development with special emphasis on proliferation, apoptosis and also the serotonin receptor 5HT-2A. Opercular formation was evident on 21-week gestation, shortly followed by appearance of gyri in the insula. At this time point, a shift from proliferative toward apoptotic cells was evident up to 32 weeks of gestation. In this week, immunoreactivity for 5HT-2A became obvious. Taken together, the authors stated that their findings appoint to an earlier differentiation of the insula, compared to many other parts of the human cerebral cortex.

The vitamin D binding protein (DBP) is secreted from hepatocytes and functions to bind and transport the steroid prohormone vitamin D3 from the place of the cutaneous synthesis into circulation (Gallieni et al. 2009). Jirikowski et al. (2009) now observed DBP-expressing neurons in the rat hypothalamus. Part of the supraoptic and of the paraventricular neurons as well as widespread axonal projections throughout the lateral hypothalamus, the median eminence and the posterior pituitary lobe showed DBP immunoreactivity. Immunopositive cells were also detected in choroid plexus epithelium and in some of the endocrine cells in the anterior pituitary lobe. ISH also indicated an intrinsic expression of DBP in the rat hypothalamus and that DBP might be transported along with the classical neurohypophyseal hormones.

Tyrosine hydroxylase (TH) is the rate-limiting enzyme in the biosynthesis of catecholamines. The developmental expression of the two genes coding TH in zebrafish has recently been mapped by Chen et al. (2009). In the developing brain, TH1 mRNA signals were detected as early as 1-day post-fertilization. In adult zebrafish, TH1 mRNA was more abundant than TH2 mRNA in the brain and eyes, whereas TH2 mRNA was more abundant in the periphery, including liver, kidney and heart.

Neural tube defects are among the most distressing congenital anomalies, mostly emerge from failure of neural tube closure and are associated with high homocysteine levels (Varela-Moreiras et al. 2009). Maternal ingestion of folic acid (FA) reduces neural tube defects. Kobus et al. (2009) studied the effects of FA and homocysteine on cell proliferation, adhesion, as well as apoptosis during spinal development in chicken embryos. Homocysteine-treated embryos and also six of ten embryos treated with FA and homocysteine showed failure of closure of the neural tube. Detailed investigations unraveled that homocysteine decreased the thickness of the mantle and marginal layers of the spinal cord. FA was ineffective to prevent this effect, but reversed the decrease of proliferating cells in the spinal cord induced by homocysteine and also led to the highest density of apoptotic cells. The authors' findings confirmed that a fine-tuned balance between FA and homocysteine levels is needed for spinal cord development.

Peripheral, myenteric and sensory neuronal system

Pulmonary neuroepithelial bodies (NEBs) are highly specialized and diffusely spread groups of pulmonary neuroendocrine cells. These cells are thought to possess oxygen-sensing capabilities and to potentially guard lung stem cell niches (Sorokin et al. 1997). Brouns et al. (2009) characterized the neurochemical innervation pattern of NEB in mouse lungs. NEBs were contacted by a plethora of nerve fiber populations, and the authors found that NEBs received intraepithelial nerve terminals of at least two different populations of myelinated vagal afferents, which either (i) were immunoreactive for vesicular glutamate transporters and calbindin D or (ii) expressed P2X(2) and P2X(3) ATP receptors. Calcitonin gene-related peptide immunoreactivity was seen in varicose vagal nerve fibers in close proximity to NEBs. The authors' work might be seen as a first step toward deciphering the innervation and function of NEBs which probably fulfill various functions in normal airways.

Lindig et al. (2009) recently compared the morphology of stubby and spiny myenteric neurons derived from the human small intestine. Immunohistochemical triple staining for leu-enkephalin (to visualize neurons with stubby-shaped dendrites), vasoactive intestinal peptide (to detect spiny-shaped dendrites) and neurofilaments (as a general marker for enteric neurons) together with software-based three-dimensional reconstructions led to impressive images of myenteric neurons. The authors found that most dendrites of stubby neurons emerged only from the somal circumference, whereas in spiny neurons they also emerged from the luminal somal surface. The volumes of spiny neurons were significantly larger and had more dendrites than those of stubby neurons. This work is a further step toward understanding differences between stubby and spiny neurons.

Several recent studies examined the distribution of purinoreceptors in different neurons (Banerjee et al. 2009; Guo et al. 2009; Kestler et al. 2009; Suzuki-Kerr et al. 2009). Two major families of purinoceptors have been identified as P1 and P2, respectively (Nakatsuka and Gu 2006). The P2 receptors fall into two families, P2X and P2Y, and the P2X receptors are ligand-gated cation channels (Nakatsuka and Gu 2006). Kestler and co-workers studied the distribution of the P2X3 receptor isoform in myenteric ganglia of the mouse esophagus. For these cells, intraganglionic laminar endings (IGLEs) represent the major vagal afferent terminals. In most of the esophageal IGLEs, colocalization with P2X3 and P2X2 was found, suggesting the occurrence of heteromeric P2X2/3 receptors. P2X3 also was detected in ~80% of myenteric ganglia in the mouse. In another study, differential expression of P2X receptors 2, 4, 5 and 6 on vasopressin- and oxytocin-containing neurons in supraoptic and paraventricular nuclei of rat hypothalamus was

described (Guo et al. 2009). In the rat lens, differential membrane redistribution of P2X receptor isoforms in response to osmotic and hyperglycemic stress was found by Suzuki-Kerr et al. (2009). In response to hypertonic stress, P2X1 and 4 became more closely associated with the broad sides of fiber cells, whereas under hypotonic conditions P2X4 and 6 associated with the narrow side membranes. No changes in subcellular distribution were observed for P2X2, 3 and 7 isoforms. These findings led the authors to conclude that P2X receptors could be differentially recruited to specific membrane domains of lens fiber cells in response to stress situations. Banerjee et al. (2009) finally reported an altered expression of P2X3 in vagal and spinal afferents following esophagitis in rats. The authors demonstrated an upregulation of P2X3 and its co-localization with TRPV1 receptor in vagal and spinal afferents of chronic esophagitis, and argued that this process might contribute to esophageal hypersensitivity in this condition.

TRP channels of the TRPV, TRPA and TRPM subfamilies are involved in somatosensation, including nociception. However, little is known about the distribution of TRPC channels in rat sensory neurons. Kress et al. (2008) worked on TRPC channels in dorsal root ganglion neurons. Six out of seven known TRPC subtypes were expressed in lumbar DRG, with TRPC1, 3 and 6 being the most abundant subtypes. A pharmacological activator of the TRPC3 and 6 subtypes, oleylacylglycerol, led to an increase in intracellular Ca^{2+}. Intriguingly, inhibitors of TRPV1 blocked oleylacylglycerol-induced rise of Ca^{2+}, supporting that TRPV1 and TRPC variants are important for Ca^{2+} homeostasis in rat sensory neurons.

The chemosensory Grueneberg ganglion (GG) is a cluster of neurons localized to the vestibule of the anterior nasal cavity (Eid and Cortright 2009). Recently, it was observed that in mice, GG neurons respond to cool ambient temperatures. Reception of coolness is mediated by TRPM8 in mammals but by cGMP pathways in nematodes (Tobin and Bargmann 2004). Because no signs of TRPM8 expression were found in GG, Fleischer et al. (2009) studied cGMP signaling elements in this ganglion. A great number of solely GG neurons expressed the transmembrane guanylyl cyclase subtype GC-G. The authors also observed that coolness-stimulated responses were detected only in neurons expressing the olfactory receptor V2r83 and the phosphodiesterase PDE2A. In GG, consequently, various similarities to thermosensation of neurons of *C. elegans* were found.

Merkel cells (MCs) are neuroendocrine cells of the skin. Eispert et al. (2009) recently used markers for N-CAM, NGF receptor, neurofilaments and synaptophysin to detect different MC populations in different parts of the epidermis. Although being positive for markers for epithelial as well as neural cells, putative MC subpopulations have been found, and potential functions were discussed.

Two recent articles aimed at identifying distinct molecules in the rat cochlea. Dlugaiczyk et al. (2008) focused on glycine receptors and gephyrin, and found that GlyRα3, GlyRβ and gephyrin were expressed in the organ of Corti and spiral ganglion neurons in RT-PCR, ISH and IHC experiments. Also two alternative splice variants of GlyRα3 were detected. These findings led the authors to speculate that these inhibitory receptors might serve as target molecules of the efferent olivocochlear bundle. On the other hand, Su et al. (2008) presented the novel finding of the localization of the transmembrane inner ear expressed (Tmie) protein in rat cochlea. Tmie was localized in the spiral limbus, spiral ligament, organ of Corti and stria vascularis. Interestingly, mutations of the Tmie gene have been shown to be associated with deafness in humans (Naz et al. 2002).

Pathological conditions and models

Cancer

De Wever et al. (2008) provided a comprehensive review on molecular mechanisms and characteristics underlying epithelial–mesenchymal transition (EMT). In EMT, epithelial cells lose many of their epithelial characteristics and acquire properties that are fundamental for mesenchymal cells. Cellular and molecular details of EMT signatures and footprints were summarized which include silencing of cell adhesion molecules and activation of MMPs or vimentin. In another recent study, downregulation of laminin α5 and upregulation of laminin α4 during EMT has been found (Takkunen et al. 2008). De Wever and co-workers also mentioned special transcription factors, for examples transcriptional repressors of E-cadherin transcription, such as Snail, Slug, and others in their review, which have also relevance for chemotherapy treatments. Upregulation of Snail in myofibroblast-like cells of oral squamous cell carcinoma was reported by Franz et al. (2009) recently. Similar to Snail, the metastasis-associated genes MTA1 and MTA3s are upregulated during EMT and in human placenta and chorionic carcinoma cells (Bruning et al. 2009).

Working with the tumorigenesis model of the mammary gland, Ghajar and Bissell (2008) provided an enlightening review about the ECM control of mammary gland morphogenesis. The authors described how molecular components of the ECM direct mammary gland formation and also discussed pathophysiological inabilities to interpret and process ECM signals, which might lead to disorganization and malignancy. These insights, however, could also be used to reprogram aberrant epithelial cells. Again, the technical progress in intravital and multiphoton fluorescence imaging

have led to compelling new findings of these dynamic processes.

Lorusso and Ruegg (2008) wrote a detailed review on the tumor microenvironment and its contribution to tumor evolution toward metastasis. The authors critically noted that the formation of a clinically relevant tumor requires support from the surrounding normal stroma with important roles for carcinoma-associated fibroblasts, leukocytes, bone marrow-derived cells, blood- and lymphatic vascular endothelial cells. These dynamic and reciprocal interactions between tumor cells and cells of the tumor microenvironment with its molecular key components were introduced and emerging attractive targets for therapeutic strategies were also explained.

Chick embryo model systems involving the technique of chorioallantoic grafting have provided important insights into tumor development, angiogenesis and tumor cell dissemination (Deryugina and Quigley 2008). The ability of the chick embryo's chorioallantoic membrane (CAM) to efficiently support the growth of inoculated xenogenic tumor cells is ideally suited to study human tumor cell metastasis. Deryugina and Quigley (2008) recently summarized current knowledge gained by this technique. Because of its high degree of vascularization, CAM sustains rapid tumor formation within several days following cell grafting. Moreover, the CAM's dense capillary network can function as a target of aggressive tumor cells trying to escape from the primary tumor, thereby giving the researchers ideal read-out possibilities to investigate metastasis formation. The authors also pointed to the use of the CAM capillary system as a place for initial arrest and cell extravasation, after intravenous inoculation of tumor cells. All this makes the CAM not only an attractive but also microscopically easily accessible tool for studying grafted tumor cells. Another setup for studying cancer growth and invasion has been developed by Alexander et al. (2008). The authors used a modified mouse skin-fold chamber for orthotopic implantation, growth and invasion of human HT-1080 fibrosarcoma cells. These cells express different GFP-variant proteins in either cytoplasm or nucleus and are ideally suited to reconstruct tumor cell behavior by epifluorescence and multiphoton microscopy (Yamamoto et al. 2003). Their setup allowed the authors to investigate several types of cell invasion, including single cell, diffuse collective or collective strand invasion with high structural precision.

Prostasin is a glycosylphosphatidylinositol-anchored serine proteinase. Recently, data for prostate and breast cancer demonstrated the potential of prostasin as a suppressor of invasion because overexpression of human prostasin led to reduced cell invasiveness in vitro (Chen et al. 2001). Ma et al. (2009) lately demonstrated that prostasin inhibited cell invasion in human choriocarcinomal cells. This research was based on the assumption that controlled invasion of the uterine wall by trophoblast cells is pivotal for successful pregnancy. Prostasin was expressed at a relatively high level in human placenta trophoblasts in early pregnancy. In cultured human choriocarcinomal JEG-3 cells, treatment with a function-blocking antibody against prostasin led to upregulation of MMPs and TIMPs and enhanced cell invasion. These findings were interpreted to confirm the hypothesis that prostasin might function to avoid overshooting penetration of the trophoblast into the uterine wall.

As already noted, proteinases possess crucial functions for invasion of cells. In an attempt to search for MMP-inducing factors, CD147, also known as extracellular matrix metalloproteinase inducer (EMMPRIN), was identified (Nabeshima et al. 2006). In a spontaneous rat metastasis model, Donadio et al. (2008) characterized the roles of EMMPRIN and MMPs as regulators of tumor–host interactions. Increased proMMP-9 expression in metastasized liver and spleen samples from tumor-bearing rats were found concomitantly with EMMPRIN-positive tumor cells in these tissues. Moreover, endogenous EMMPRIN expression of hepatocytes was also induced. In vitro studies showed that EMMPRIN upregulation was dependent on tumor–host cell but not tumor–ECM interactions. The authors' findings proposed EMMPRIN as a new target for therapeutic interventions against tumors.

In recent years, various studies have identified novel markers in distinct cancer subtypes. Emerging evidence suggests a role for glutamate and its receptors in cancer cells (Shin et al. 2008b). Stepulak et al. (2009) designed a study to systematically analyze the expression of ionotropic and metabotropic glutamate receptor subunits in several human cancer cell lines. All glutamate receptor subunits investigated were differentially expressed in tumor cell lines. Interestingly, expression levels of glutamate receptor subunits NR2B, GluR4, GluR6 and KA2 were lower in the majority of tumors as compared to human brain tissue. Electrophysiological experiments also showed that at least some cell lines depolarized in response to application of glutamate agonists, indicating the formation of functional channels. Future studies have to explore the potential role of these glutamate receptor antagonists in cancer therapy. Daskalow et al. (2009) focused on the sixth most frequent human cancer worldwide, hepatocellular carcinoma (HCC). Glycolysis is known as a potent driving force not only for tumor growth but also for therapy failure. Several central glycolysis-related factors, including Glut-1 and Glut-2, phosphoglycerate kinase-1 (PGK-1) and hypoxia-inducible factor-1α (HIF-1α), were studied in various benign and malignant human liver samples in this study. Glut-1 protein was absent, and HIF-1α was identified in only 12% of HCC samples. PGK-1 expression was very intense in HCC, and

Glut-2 was expressed in half of the HCC cases. However, both markers were associated with poor prognosis for patients. In another study, Gramann et al. (2009) reported a strong collagen VI expression which is commonly associated with aggressive tumor growth in juvenile angiofibromas (JA). JAs are rare fibrovascular neoplasms developing mostly in the posterior nasal cavity of adolescent males (Coutinho-Camillo et al. 2008).

Ten Dem and co-workers used a novel antibody (GD3A12) derived from phage display which is directed against dermatan sulfates rich in IdoA-GalNAc4S disaccharide units. This antibody was used to investigate normal and diseased human tissue (Ten Dam et al. 2009). GD3A12-positive signals were mainly confined to connective tissues of most examined organs with a fibrillar-type of staining. In ovarian carcinomas, strong dermatan sulfate immunoreactivity was found not only in the stromal parts but also to a minor extend on tumor cells. Future studies have to show whether this unique dermatan sulfate antibody might be useful to investigate specific dermatan sulfate domains in healthy and diseased conditions.

Two recent studies focused on glycodelins (Gds) in diseased conditions. Gds are glycoproteins displaying a gender-specific glycosylation and various functions for cell recognition (for example as T-cell inhibitors) and differentiation (Seppala 1999). Gd A is primarily produced in endometrial and decidual tissues and secreted into the amniotic fluid. With the help of a novel Gd antibody, Jeschke et al. (2009) studied Gd localization in serous, mucinous, endometrioid and clear cell ovarian tumors. A Gd isoform was also purified from ascites fluid of ovarian cancer patients but showed significant differences in sialyl Lewis-type oligosaccharides as compared to Gd A. Interestingly, this Gd isoform inhibited IL-2-induced proliferation of peripheral blood leukocytes. The immunomodulatory effect of Gd was further found in ovalbumin-induced allergic airway inflammation, an experimental rat model of allergen-induced airway inflammation (Kunert-Keil et al. 2009). Kunert-Keil and co-workers examined the distribution of Gd mRNA and protein by ISH and IHC, respectively, and found Gd to be expressed in Clara cells of bronchial epithelium, type II pneumocytes and alveolar macrophages. As expected by the authors, an increase in Gd mRNA and protein in rat lungs after ovalbumin challenge was seen.

Cxs of GJs have been shown to possess both tumor-suppressive and tumor-promoting functions (Vinken et al. 2006). Gotow et al. (2008) characterized the role of GJs in a special rat strain which is insensitive to the hepatocarcinogen 3′-methyl-4-dimethylaminoazobenzene (3′-MeDAB) (DRH rats), compared to the 3′-MeDAB-sensitive parental strain of Donryu rats. In control conditions, hepatic GJs and Cx32 protein expressions were higher in DRH rats than in control Donryu rats. Following a diet containing 3′-MeDAB, GJs and Cx32 increased significantly in Donryu rats, but signs of tumor activity were only significantly increased in these rats, indicating that DRH rats were less susceptible to 3′-MeDAB. These findings led the authors to speculate that the resistance of DRH rats to carcinogenesis may at least partially be due to their stabilized GJs, which could coordinate metabolic coupling, and therefore evade 3′-MeDAB toxicity.

Atherosclerosis

Many steps of the pathogenesis of atherosclerosis are still not resolved. It is, however, known that coagulation and also fibrinolysis are involved in the initiation and progression of atherosclerosis (Libby et al. 2006). Fibrinogen, fibrin and fibrin(ogen) degradation products are known components of atherosclerotic plaques (Libby et al. 2006). Argraves et al. (2009) recently further characterized deposition patterns of fibulin-1 and fibrinogen in human atherosclerotic lesions. In normal blood vessels, the fibrinogen-binding protein fibulin-1 is a component of the ECM (Tran et al. 1995). Both proteins were found by the authors to colocalize in atherosclerotic lesions and regions of fresh thrombi. Fibulin-1 signals were especially strong in lesion areas rich in macrophages and foam cells, and strong ECM deposition of fibulin-1 was observed in acellular atheromatous and myxomatous regions. Possible origins of lesion-associated fibulin-1 were discussed by the authors. Wookey et al. (2009) investigated the expression of the calcitonin receptor by cells recruited into the endothelial layer and neointima of atherosclerotic plaques of rabbits fed a cholesterol-supplemented diet for 4 weeks. Immunosignals specific for the calcitonin receptor were located deep into atherosclerotic plaques as well as within the endothelial layer of the neointima. The authors further succeeded in showing that calcitonin receptor signals were markedly reduced in the stabilized fibrous cap of plaques after a 12-week period of normal diet. This led the authors to speculate that the calcitonin receptor is involved in primary pathogenic events but, as stabilization of plaque progresses, it becomes downregulated.

Fibrotic disorders

Epithelial–mesenchymal transition has been considered to be involved in organ fibrogenesis (Guarino et al. 2009). In a recent study by Yamada et al. (2008), the authors, however, found contradicting data in the pathophysiology of pulmonary fibrosis. The authors performed dual-IHC to assess the coexpression of epithelial (E-cadherin, T1α) and mesenchymal (α-smooth muscle actin, vimentin) markers in lung tissues from a mouse model of pulmonary fibrosis and from patients with idiopathic pulmonary fibrosis. Nevertheless,

the authors did not find indications for such double positive cells in the tissues investigated. The authors argued that EMT either takes place during a very short, and thus undetectable time period or that it is not necessary for the development of pulmonary fibrosis in vivo. Xia et al. (2009) investigated the inflammatory and fibrotic response in a mouse model of myocardial fibrosis (transverse aortic constriction) which is essential to many cardiac diseases. After constriction, mouse hearts exhibited induction of chemokines and proinflammatory cytokines, upregulation of TGF-β isoforms, induction of ECM proteins, but these effects decreased after 28 days. At this time point, the authors detected fibrosis which was associated with malfunctions of the heart. The authors proposed that these studies should lay the foundations for further experiments exploring the pathogenesis of fibrotic cardiac remodeling with the whole toolbox of genetically modified mice. Many renal diseases result in end-stage glomerulosclerosis and tubulointerstitial fibrosis as main causes for renal dysfunction. Tubulointerstitial fibrosis is followed by infiltration of leukocytes and macrophages (Anders et al. 2003). Tamura et al. (2009) further examined this process in an adenine-induced tubulointerstitial nephritis mouse model, whose pathogenesis is not understood at the moment. In mice fed with an adenine-rich diet elevation of serum creatinine levels and loss of body weight were observed, suggesting the development of typical renal dysfunctions. Interestingly, the upregulation of certain cytokines was associated with a remarkable infiltration of macrophages into the tubulointerstitial area. The authors speculated that macrophage infiltration is one of the triggers initiating interstitial fibroblast activation and collagen deposition which finally results in renal dysfunction. Picard et al. (2008) studied tubulo-intestinal fibrosis in the model of unilateral ureter obstruction in the rat. It has been proposed that myofibroblasts in chronic renal failure originate from the transformation of tubular epithelial cells via EMT or from infiltration by bone marrow-derived precursors (Guarino et al. 2009). The authors questioned whether rather a transformation of resident fibroblasts into myofibroblasts takes place in renal fibrosis. In their model mice, increased protein expression of α-smooth muscle actin was revealed in resident fibroblasts by immunofluorescence studies. Inversely, a decreased expression of 5′-nucleotidase, a marker of renal cortical fibroblasts, was detected. Again, no signs of EMT were detected (see also the study by Yamada et al. 2008). Renal tubules underwent severe regressive changes, but the cells retained their epithelial characteristics indicating that resident fibroblasts were crucially involved in fibrosis in that model.

It is still not clear how kidney cysts are formed, although many genes are mutated in various forms of cystic kidney diseases (Wilson and Goilav 2007). Osten et al. (2009) used a mouse model of type 3 nephronophthisis, a form of recessive polycystic kidney disease, to show that doxycycline accelerates renal cyst growth and fibrosis. This effect was independent of Timp-2, a known inhibitor of MMPs, which is also activated by doxycycline. Experiments investigating the Ca^{2+} response of LLC-PK(1) cells treated with the urine of control or doxycycline-treated mice led to the identification of an unknown heat-labile substance which appeared to be responsible for the induction of a Ca^{2+} response. The authors cautioned that their data might explain unexpected results in phenotypes of animal models based upon doxycycline-inducible transgene expression.

Neuropathological disorders

Amyotrophic lateral sclerosis (ALS) is a rare motor neuron disorder with a yearly incidence of 1–2 per 100,000 people and highlighted by an irreversible and progressive degeneration of motoneurons (Talbot and Ansorge 2006; Valdmanis et al. 2009). The molecular pathogenesis of ALS is, however, still unknown. Petri et al. (2009) studied the expression of fibroblast growth factor (FGF)-2 and FGF receptor 1 in brain and spinal cord of ALS patients assuming that altered trophic support of motoneurons might account for impaired motoneuron functions in this disease. Therefore, post-mortem specimens of ALS patients were analyzed by RT-PCR studies and ISH. Nevertheless, the distribution and rate of cells expressing FGF-2 and FGFR1 transcripts showed no differences between ALS and control groups indicating that expression of these genes is still preserved in end stage ALS.

In the rat brain, stigmoid bodies (STBs) are spherical neurocytoplasmic inclusions containing huntingtin-associated protein 1 (HAP1) (Fujinaga et al. 2007; Takeshita et al. 2006). STBs are believed to play a protective role in polyglutamine diseases such as Huntington's disease, but are often confused with aggresomes which are different types of inclusion bodies observed in these diseases (Singhvi and Garriga 2009). Fujinaga et al. (2009) immunohistochemically compared STBs and aggresomes in the rat brain and culture cells transfected with HAP1. The authors found that after HAP1 transfection, STBs were formed from multiple fusions of small HAP1 inclusions in a microtubule-dependent process. No positive immunolocalization with aggresomal marker such as ubiquitin or IFs was found. Defects in IFs account for a wide variety of human diseases (Omary 2009). Mallory bodies (MBs) represent keratin-rich inclusion bodies observed in human alcoholic liver disease (Strnad et al. 2008). Hirano et al. (2009) now presented a novel cell culture system (AQP2- or α1-antitrypsin-transfected clone 9 hepatocytes) for the induction and study of MBs. With this system, the authors found that MBs and aggresomes represent different types of inclusion bodies.

Infectious diseases

Viral budding of hepatitis C virus (HCV) can be mimicked and viewed by EM in a model system, where HCV core proteins are overproduced with a Semliki forest virus replicon vector (Blanchard et al. 2003). In a short report, Roingeard et al. (2008) now visualized this process by three-dimensional EM. Because LDs have recently been shown to be involved in HCV virus production, the authors investigated the interaction between HCV-like particles and LDs. It was observed that the budding of HCV-like particles was mostly initiated at membranes close to LDs rather than at membranes directly opposed to LDs.

Trypanosoma cruzi is the etiologic agent of Chagas disease. Trypanosomatid parasites have different developmental stages that represent an adaptation to the different environments encountered in their two hosts, the mammalian host and the insect vector. Sant'Anna et al. (2008) recently reported that also the mammalian *T. cruzi* developmental forms have lysosome-related organelles. In their paper, the authors demonstrated that trypomastigotes and amastigotes which are the mammalian forms of *T. cruzi*, concentrate the protease cruzipain and its natural inhibitor chagasin as well as serine carboxypeptidase and a P-type proton ATPase in acidic compartments named reservosomes in other *T. cruzi* stages. In EM studies, these organelles were found at the posterior region of the parasite body with different sizes and shapes. Cavalcanti et al. (2008) focused on another organelle of trypanosomatid protozoa, the kinetoplast. The kinetoplast is an enlarged portion of a mitochondrial DNA-containing organelle. The kinetoplast DNA (kDNA) of trypanosomatids is an unusual arrangement of circular basic molecules forming a single network within the kinetoplast matrix (Shlomai 2004). In trypanosomatids harboring an endosymbiotic bacterium, the kDNA fibers display a looser arrangement. The authors have now shown that in these species, DNA and basic proteins are also located in a region between the kDNA and the inner mitochondrial membrane, termed the kinetoflagellar zone. The authors also compared these findings with the kinetoplast organization of *Bodo* sp. which represents an evolutionary ancestor of the Trypanosomatidae family.

Diabetic nephropathy is an important chronic complication of diabetes mellitus and involves many factors including hyperglycemia, growth factors, inflammatory cytokines, and lipid deposits (Conway and Maxwell 2009; Maeda 2008). Jun et al. (2009) recently investigated the role of a transcription factor regulating synthesis of triglycerides, sterol regulatory element binding protein-1 (SREBP-1), in diabetic renal tubular lipid accumulation. The authors used type 1 diabetic rats and RNAi studies in a human renal proximal tubular epithelial cells line. In animal experiments, both triglyceride and SREBP-1 were upregulated in proximal tubules of diabetic rats, which was confirmed in cell culture experiments after transfection with a SREBP-1 construct. Also, an upregulation of TGF-β1 and fibronectin was reported. The authors also successfully validated short hairpin RNA constructs targeting SREBP-1 which were interpreted as promising tool for future experiments.

Disease models and other pathological processes

Polycystic liver disease (PCLD) is a rare autosomal dominantly inherited disorder (mutations in either hepatocystin or Sec63p) that is associated with fluid-filled cysts throughout the liver (Tahvanainen et al. 2005). Waanders et al. (2008) analyzed subcellular and cellular localization of the disease-bearing proteins hepatocystin and Sec63p in fetal liver, PCLD liver and normal adult liver. Hepatocystin- and Sec63p protein expression was predominantly found in the ER. Interestingly, the majority of cysts from hepatocystin mutation carriers did not express hepatocystin, whereas Sec63p expression was found in all cyst epithelia. These findings were interpreted to indicate that cyst formation in PCLD results from a cellular recessive mechanism involving loss of hepatocystin.

Juvenile polyps are hamartomatous polyps of the colon and are characterized by mucus-filled glands and inflammatory cells and prominent stroma. About 40% of sporadic and familial cases are caused by mutations in members of the TGF-β pathway (Merg and Howe 2004). Barros et al. (2009) lately focused on the homeobox transcription factor CDX2 (as a master gene in intestinal differentiation) and on MUCs as intestinal differentiation markers in solitary juvenile polyps. The authors observed that juvenile polyps downregulated CDX2 and SMAD4, but had de novo expression of MUC5AC.

Rocha et al. (2009) examined the neurotoxic effects of mastoparan Polybia-MPII at the murine neuromuscular junction. Polybia-MPII can be isolated from the crude venom of the swarming wasp *Polybia paulista*. In EM and ICC, both volumes and density of synaptic vesicles were greatly reduced after injection of Polybia-MPII in mice. Moreover, colabeling of motor end plates with acetylcholine receptors and synaptophysin was dramatically reduced. However, these effects were very transient and disappeared after 3 days, leading the authors to speculate that this neuropathologic effect is not of clinical significance.

Surgical ablation of synergistic muscles is used in a compensatory skeletal muscle hypertrophy model in rats, which substantially increases muscle mass after few weeks (Timson et al. 1985). This model has been intensively characterized by Tamaki et al. (2009b) recently. Anabolic androgenic steroids (AAS) are widely abused by athletes and bodybuilders to manipulate their physical performance.

In their recent study, Tamaki et al. (2009a) used their compensatory muscle hypertrophy model to investigate the role of the AAS nandrolone decanoate. Although muscle wet weight gain did not differ between the groups, the authors found significantly reduced mitotic activity associated with reduced necrosis in the steroid group during the first week.

Di-(2-ethylhexyl)-phthalate (DEHP) is a plasticizer employed and released by polyvinylchloride, which is able to cross the placental barrier, and may therefore also affect breast feeding (Cimini et al. 1994). DEHP administration to mother rats increased the activities of several liver and kidney enzymes in sucklings resulting in lethal growth retardations. Rosicarelli and Stefanini (2009) recently characterized DEHP effects on histology and cell proliferation in lungs of newborn rats. The authors undertook these studies because DEHP is known to be released by medical devices utilized for pulmonary ventilation of pre-term newborns. In their current study, pregnant rats were fed with DEHP in the last week of pregnancy. In newborns, altered proliferation rates of pulmonary epithelial cells together with a reduction of the gas-exchange surface were observed. The authors clearly demonstrated that in DEHP-treated newborns the alveolarization process is dramatically altered. In another study, Zei et al. (2009) studied DEHP effects on retinal vessels in newborn rats. Extensive vascular remodeling after DEHP exposure again pointed to the severe and pathogenic effects of DEHP during perinatal development of various tissues.

In a subgroup of activated macrophages, tartrate resistant acid phosphatase (TRAP) is highly expressed (Hayman et al. 2001). Lang et al. (2009) tested the induction and cellular expression of TRAP during dextran sodium sulfate-induced colitis in rats. In the early stage of acute colitis, an increase of certain cytokines and a minimal increase of TRAP immunolabeling in macrophages of the upper lamina propria was seen. In in vitro studies using a monocyte/macrophage cell line, tumor necrosis factor α also upregulated TRAP expression. In later phases, which were accompanied by fulminant colitis, a massive infiltration of macrophages was observed in the lower part of the lamina propria and in the submuscular layer. Detailed analysis of expression of pro- and mature TRAP isoforms indicated that these macrophages provided a source of replenishment of cells located in the upper lamina propria.

References

Al-Amoudi A, Diez DC, Betts MJ, Frangakis AS (2007) The molecular architecture of cadherins in native epidermal desmosomes. Nature 450:832–837

Alexander S, Koehl GE, Hirschberg M, Geissler EK, Friedl P (2008) Dynamic imaging of cancer growth and invasion: a modified skin-fold chamber model. Histochem Cell Biol 130:1147–1154

Alieva IB, Uzbekov RE (2008) The centrosome is a polyfunctional multiprotein cell complex. Biochemistry 73:626–643

Anders HJ, Vielhauer V, Schlondorff D (2003) Chemokines and chemokine receptors are involved in the resolution or progression of renal disease. Kidney Int 63:401–415

Angermuller S, Islinger M, Volkl A (2009) Peroxisomes and reactive oxygen species, a lasting challenge. Histochem Cell Biol 131:459–463

Argraves WS, Tanaka A, Smith EP, Twal WO, Argraves KM, Fan D, Haudenschild CC (2009) Fibulin-1 and fibrinogen in human atherosclerotic lesions. Histochem Cell Biol 132(5):559–565

Asan E, Drenckhahn D (2008) State-of-the-art technologies, current opinions and developments, and novel findings: news from the field of histochemistry and cell biology. Histochem Cell Biol 130:1205–1251

Banerjee B, Medda BK, Schmidt J, Zheng Y, Zhang Z, Shaker R, Sengupta JN (2009) Altered expression of P2X(3) in vagal and spinal afferents following esophagitis in rats. Histochem Cell Biol (in press)

Baratta JL, Ngo A, Lopez B, Kasabwalla N, Longmuir KJ, Robertson RT (2009) Cellular organization of normal mouse liver: a histological, quantitative immunocytochemical, and fine structural analysis. Histochem Cell Biol 131:713–726

Bareiss PM, Metzger M, Sohn K, Rupp S, Frick JS, Autenrieth IB, Lang F, Schwarz H, Skutella T, Just L (2008) Organotypical tissue cultures from adult murine colon as an in vitro model of intestinal mucosa. Histochem Cell Biol 129:795–804

Barros R, Mendes N, Howe JR, Reis CA, de Bolos C, Carneiro F, David L, Almeida R (2009) Juvenile polyps have gastric differentiation with MUC5AC expression and downregulation of CDX2 and SMAD4. Histochem Cell Biol 131:765–772

Batoni G, Maisetta G, Esin S, Campa M (2006) Human beta-defensin-3: a promising antimicrobial peptide. Mini Rev Med Chem 6:1063–1073

Baumer Y, Burger S, Curry FE, Golenhofen N, Drenckhahn D, Waschke J (2008a) Differential role of Rho GTPases in endothelial barrier regulation dependent on endothelial cell origin. Histochem Cell Biol 129:179–191

Baumer Y, Drenckhahn D, Waschke J (2008b) cAMP induced Rac 1-mediated cytoskeletal reorganization in microvascular endothelium. Histochem Cell Biol 129:765–778

Belazi D, Sole-Domenech S, Johansson B, Schalling M, Sjovall P (2009) Chemical analysis of osmium tetroxide staining in adipose tissue using imaging ToF-SIMS. Histochem Cell Biol 132:105–115

Ben David D, Reznick AZ, Srouji S, Livne E (2008) Exposure to pro-inflammatory cytokines upregulates MMP-9 synthesis by mesenchymal stem cells-derived osteoprogenitors. Histochem Cell Biol 129:589–597

Benham CD, Gunthorpe MJ, Davis JB (2003) TRPV channels as temperature sensors. Cell Calcium 33:479–487

Berg KD, Tamas RM, Riemann A, Niels-Christiansen LL, Hansen GH, Michael Danielsen E (2009) Caveolae in fibroblast-like synoviocytes: static structures associated with vimentin-based intermediate filaments. Histochem Cell Biol 131:103–114

Bingle CD, Craven CJ (2002) PLUNC: a novel family of candidate host defence proteins expressed in the upper airways and nasopharynx. Hum Mol Genet 11:937–943

Bingle L, Barnes FA, Lunn H, Musa M, Webster S, Douglas CW, Cross SS, High AS, Bingle CD (2009) Characterisation and expression of SPLUNC2, the human orthologue of rodent parotid secretory protein. Histochem Cell Biol 132:339–349

Blanchard E, Hourioux C, Brand D, Ait-Goughoulte M, Moreau A, Trassard S, Sizaret PY, Dubois F, Roingeard P (2003) Hepatitis C virus-like particle budding: role of the core protein and importance of its Asp111. J Virol 77:10131–10138

Blaschitz A, Gauster M, Dohr G (2008) Application of cryo-compatible antibodies to human placenta paraffin sections. Histochem Cell Biol 130:595–599

Bogdanovic E, Coombs N, Dumont DJ (2009) Oligomerized Tie2 localizes to clathrin-coated pits in response to angiopoietin-1. Histochem Cell Biol 132:225–237

Boisseau S, Kunert-Keil C, Lucke S, Bouron A (2009) Heterogeneous distribution of TRPC proteins in the embryonic cortex. Histochem Cell Biol 131:355–363

Borisov AB, Martynova MG, Russell MW (2008) Early incorporation of obscurin into nascent sarcomeres: implication for myofibril assembly during cardiac myogenesis. Histochem Cell Biol 129:463–478

Bottone MG, Soldani C, Fraschini A, Alpini C, Croce AC, Bottiroli G, Pellicciari C (2007) Enzyme-assisted photosensitization with rose Bengal acetate induces structural and functional alteration of mitochondria in HeLa cells. Histochem Cell Biol 127:263–271

Bottone MG, Soldani C, Fraschini A, Croce AC, Bottiroli G, Camboni T, Scovassi AI, Pellicciari C (2009) Enzyme-assisted photosensitization activates different apoptotic pathways in Rose Bengal acetate treated HeLa cells. Histochem Cell Biol 131:391–399

Boucher R, Larkin H, Brodeur J, Gagnon H, Theriault C, Lavoie C (2008) Intracellular trafficking of LRP9 is dependent on two acidic cluster/dileucine motifs. Histochem Cell Biol 130:315–327

Brandt B, Buchse T, Abou-Eladab EF, Tiedge M, Krause E, Jeschke U, Walzel H (2008) Galectin-1 induced activation of the apoptotic death-receptor pathway in human Jurkat T lymphocytes. Histochem Cell Biol 129:599–609

Brauer L, Moschter S, Beileke S, Jager K, Garreis F, Paulsen FP (2009) Human parotid and submandibular glands express and secrete surfactant proteins A, B, C and D. Histochem Cell Biol 132:331–338

Breitkreutz D, Mirancea N, Nischt R (2009) Basement membranes in skin: unique matrix structures with diverse functions? Histochem Cell Biol 132:1–10

Brouns I, Oztay F, Pintelon I, De Proost I, Lembrechts R, Timmermans JP, Adriaensen D (2009) Neurochemical pattern of the complex innervation of neuroepithelial bodies in mouse lungs. Histochem Cell Biol 131:55–74

Bruni-Cardoso A, Vilamaior PS, Taboga SR, Carvalho HF (2008) Localized matrix metalloproteinase (MMP)-2 and MMP-9 activity in the rat ventral prostate during the first week of postnatal development. Histochem Cell Biol 129:805–815

Bruning A, Makovitzky J, Gingelmaier A, Friese K, Mylonas I (2009) The metastasis-associated genes MTA1 and MTA3 are abundantly expressed in human placenta and chorionic carcinoma cells. Histochem Cell Biol 132:33–38

Burgess MD, Moore KD, Carter GM, Alli AA, Granda CS, Ichii H, Ricordi C, Gower WR Jr (2009) C-type natriuretic peptide receptor expression in pancreatic alpha cells. Histochem Cell Biol 132:95–103

Cao Y, Liu X, De Clercq E (2009) Cessation of HIV-1 transcription by inhibiting regulatory protein Rev-mediated RNA transport. Curr HIV Res 7:101–108

Carlsson L, Yu JG, Thornell LE (2008) New aspects of obscurin in human striated muscles. Histochem Cell Biol 130:91–103

Cavalcanti DP, Thiry M, de Souza W, Motta MC (2008) The kinetoplast ultrastructural organization of endosymbiont-bearing trypanosomatids as revealed by deep-etching, cytochemical and immunocytochemical analysis. Histochem Cell Biol 130:1177–1185

Cavey M, Rauzi M, Lenne PF, Lecuit T (2008) A two-tiered mechanism for stabilization and immobilization of E-cadherin. Nature 453:751–756

Cermelli S, Guo Y, Gross SP, Welte MA (2006) The lipid-droplet proteome reveals that droplets are a protein-storage depot. Curr Biol 16:1783–1795

Chen LM, Hodge GB, Guarda LA, Welch JL, Greenberg NM, Chai KX (2001) Down-regulation of prostasin serine protease: a potential invasion suppressor in prostate cancer. Prostate 48:93–103

Chen YC, Priyadarshini M, Panula P (2009) Complementary developmental expression of the two tyrosine hydroxylase transcripts in zebrafish. Histochem Cell Biol 132(4):375–381

Cheng J, Fujita A, Ohsaki Y, Suzuki M, Shinohara Y, Fujimoto T (2009) Quantitative electron microscopy shows uniform incorporation of triglycerides into existing lipid droplets. Histochem Cell Biol 132:281–291

Chiu CC, Sheu JC, Chen CH, Lee CZ, Chiou LL, Chou SH, Huang GT, Lee HS (2009) Global gene expression profiling reveals a key role of CD44 in hepatic oval-cell reaction after 2-AAF/CCl(4) injury in rodents. Histochem Cell Biol (in press)

Choi YS, Cheng J, Segre J, Sinha S (2008) Generation and analysis of Elf5-LacZ mouse: unique and dynamic expression of Elf5 (ESE-2) in the inner root sheath of cycling hair follicles. Histochem Cell Biol 129:85–94

Cimini AM, Sulli A, Stefanini S, Serafini B, Moreno S, Rossi L, Giorgi M, Ceru MP (1994) Effects of Di-(2-ethylhexyl)phthalate on peroxisomes of liver, kidney and brain of lactating rats and their pups. Cell Mol Biol 40:1063–1076

Cisterna B, Malatesta M, Dieker J, Muller S, Prosperi E, Biggiogera M (2009) An active mechanism flanks and modulates the export of the small ribosomal subunits. Histochem Cell Biol 131:743–753

Cizkova D, Soukup T, Mokry J (2009) Expression of nestin, desmin and vimentin in intact and regenerating muscle spindles of rat hind limb skeletal muscles. Histochem Cell Biol 131:197–206

Claassen H, Schicht M, Sel S, Werner J, Paulsen F (2009) The fate of chondrocytes during ageing of human thyroid cartilage. Histochem Cell Biol 131:605–614

Conway BR, Maxwell AP (2009) Genetics of diabetic nephropathy: are there clues to the understanding of common kidney diseases? Nephron Clin Pract 112:c213–c221

Conway C, Dobson L, O'Grady A, Kay E, Costello S, O'Shea D (2008) Virtual microscopy as an enabler of automated/quantitative assessment of protein expression in TMAs. Histochem Cell Biol 130:447–463

Corbeil D, Roper K, Fargeas CA, Joester A, Huttner WB (2001) Prominin: a story of cholesterol, plasma membrane protrusions and human pathology. Traffic 2:82–91

Corpa JM (2006) Ectopic pregnancy in animals and humans. Reproduction 131:631–640

Cosen-Binker LI, Kapus A (2006) Cortactin: the gray eminence of the cytoskeleton. Physiology 21:352–361

Coutinho-Camillo CM, Brentani MM, Nagai MA (2008) Genetic alterations in juvenile nasopharyngeal angiofibromas. Head Neck 30:390–400

Csaki C, Matis U, Mobasheri A, Ye H, Shakibaei M (2007) Chondrogenesis, osteogenesis and adipogenesis of canine mesenchymal stem cells: a biochemical, morphological and ultrastructural study. Histochem Cell Biol 128:507–520

Csaki C, Matis U, Mobasheri A, Shakibaei M (2009) Co-culture of canine mesenchymal stem cells with primary bone-derived osteoblasts promotes osteogenic differentiation. Histochem Cell Biol 131:251–266

Dariush Fahimi H (2009) Peroxisomes: 40 years of histochemical staining, personal reminiscences. Histochem Cell Biol 131:437–440

Daskalow K, Pfander D, Weichert W, Rohwer N, Thelen A, Neuhaus P, Jonas S, Wiedenmann B, Benckert C, Cramer T (2009) Distinct temporospatial expression patterns of glycolysis-related proteins in human hepatocellular carcinoma. Histochem Cell Biol 132:21–31

De Wever O, Pauwels P, De Craene B, Sabbah M, Emami S, Redeuilh G, Gespach C, Bracke M, Berx G (2008) Molecular and pathological

signatures of epithelial-mesenchymal transitions at the cancer invasion front. Histochem Cell Biol 130:481–494
Debbage P, Jaschke W (2008) Molecular imaging with nanoparticles: giant roles for dwarf actors. Histochem Cell Biol 130:845–875
Delille HK, Alves R, Schrader M (2009) Biogenesis of peroxisomes and mitochondria: linked by division. Histochem Cell Biol 131:441–446
Deryugina EI, Quigley JP (2008) Chick embryo chorioallantoic membrane model systems to study and visualize human tumor cell metastasis. Histochem Cell Biol 130:1119–1130
Diaz G, Batetta B, Sanna F, Uda S, Reali C, Angius F, Melis M, Falchi AM (2008) Lipid droplet changes in proliferating and quiescent 3T3 fibroblasts. Histochem Cell Biol 129:611–621
Dingova H, Fukalova J, Maninova M, Philimonenko VV, Hozak P (2009) Ultrastructural localization of actin and actin-binding proteins in the nucleus. Histochem Cell Biol 131:425–434
Dlugaiczyk J, Singer W, Schick B, Iro H, Becker K, Becker CM, Zimmermann U, Rohbock K, Knipper M (2008) Expression of glycine receptors and gephyrin in the rat cochlea. Histochem Cell Biol 129:513–523
Doak SH, Rogers D, Jones B, Francis L, Conlan RS, Wright C (2008) High-resolution imaging using a novel atomic force microscope and confocal laser scanning microscope hybrid instrument: essential sample preparation aspects. Histochem Cell Biol 130:909–916
Donadio AC, Remedi MM, Susperreguy S, Frede S, Gilardoni MB, Tang Y, Pellizas CG, Yan L (2008) Extracellular matrix metalloproteinase inducer (EMMPRIN) and matrix metalloproteinases (MMPs) as regulators of tumor-host interaction in a spontaneous metastasis model in rats. Histochem Cell Biol 130:1155–1164
Dudas J, Mansuroglu T, Batusic D, Ramadori G (2009) Thy-1 is expressed in myofibroblasts but not found in hepatic stellate cells following liver injury. Histochem Cell Biol 131:115–127
Dumic J, Dabelic S, Flogel M (2006) Galectin-3: an open-ended story. Biochim Biophys Acta 1760:616–635
Dwyer J, Li H, Xu D, Liu JP (2007) Transcriptional regulation of telomerase activity: roles of the Ets transcription factor family. Ann N Y Acad Sci 1114:36–47
Dydensborg AB, Teller IC, Basora N, Groulx JF, Auclair J, Francoeur C, Escaffit F, Pare F, Herring E, Menard D, Beaulieu JF (2009) Differential expression of the integrins alpha6Abeta4 and alpha6Bbeta4 along the crypt-villus axis in the human small intestine. Histochem Cell Biol 131:531–536
Ebnet K (2008) Organization of multiprotein complexes at cell-cell junctions. Histochem Cell Biol 130:1–20
Eid SR, Cortright DN (2009) Transient receptor potential channels on sensory nerves. Handb Exp Pharmacol (194):261–281
Eid J, Fehr A, Gray J, Luong K, Lyle J, Otto G, Peluso P, Rank D, Baybayan P, Bettman B, Bibillo A, Bjornson K, Chaudhuri B, Christians F, Cicero R, Clark S, Dalal R, Dewinter A, Dixon J, Foquet M, Gaertner A, Hardenbol P, Heiner C, Hester K, Holden D, Kearns G, Kong X, Kuse R, Lacroix Y, Lin S, Lundquist P, Ma C, Marks P, Maxham M, Murphy D, Park I, Pham T, Phillips M, Roy J, Sebra R, Shen G, Sorenson J, Tomaney A, Travers K, Trulson M, Vieceli J, Wegener J, Wu D, Yang A, Zaccarin D, Zhao P, Zhong F, Korlach J, Turner S (2009) Real-time DNA sequencing from single polymerase molecules. Science 323:133–138
Eispert AC, Fuchs F, Brandner JM, Houdek P, Wladykowski E, Moll I (2009) Evidence for distinct populations of human Merkel cells. Histochem Cell Biol 132:83–93
Emmert-Buck MR, Bonner RF, Smith PD, Chuaqui RF, Zhuang Z, Goldstein SR, Weiss RA, Liotta LA (1996) Laser capture microdissection. Science 274:998–1001
Erben RG, Odorfer KI, Siebenhutter M, Weber K, Rohleder S (2008) Histological assessment of cellular half-life in tissues in vivo. Histochem Cell Biol 130:1041–1046
Erickson HP (2007) Evolution of the cytoskeleton. Bioessays 29:668–677
Estrada R, Wang L, Jala VR, Lee JF, Lin CY, Gray RD, Haribabu B, Lee MJ (2009) Ligand-induced nuclear translocation of S1P(1) receptors mediates Cyr61 and CTGF transcription in endothelial cells. Histochem Cell Biol 131:239–249
Farragher SM, Tanney A, Kennedy RD, Paul Harkin D (2008) RNA expression analysis from formalin fixed paraffin embedded tissues. Histochem Cell Biol 130:435–445
Fink C, Weigel R, Fink L, Wilhelm J, Kliesch S, Zeiler M, Bergmann M, Brehm R (2009) Claudin-11 is over-expressed and dislocated from the blood-testis barrier in Sertoli cells associated with testicular intraepithelial neoplasia in men. Histochem Cell Biol 131:755–764
Fleischer J, Mamasuew K, Breer H (2009) Expression of cGMP signaling elements in the Grueneberg ganglion. Histochem Cell Biol 131:75–88
Forster C (2008) Tight junctions and the modulation of barrier function in disease. Histochem Cell Biol 130:55–70
Franz M, Spiegel K, Umbreit C, Richter P, Codina-Canet C, Berndt A, Altendorf-Hofmann A, Koscielny S, Hyckel P, Kosmehl H, Virtanen I (2009) Expression of Snail is associated with myofibroblast phenotype development in oral squamous cell carcinoma. Histochem Cell Biol 131:651–660
Frey S, Richter RP, Gorlich D (2006) FG-rich repeats of nuclear pore proteins form a three-dimensional meshwork with hydrogel-like properties. Science 314:815–817
Frotscher M, Zhao S, Graber W, Drakew A, Studer D (2007) New ways of looking at synapses. Histochem Cell Biol 128:91–96
Fu Y, Tang H, Huang Y, Song N, Luo Y (2009) Unraveling the mysteries of endostatin. IUBMB Life 61:613–626
Fujimoto T, Ohsaki Y, Cheng J, Suzuki M, Shinohara Y (2008) Lipid droplets: a classic organelle with new outfits. Histochem Cell Biol 130:263–279
Fujinaga R, Yanai A, Nakatsuka H, Yoshida K, Takeshita Y, Uozumi K, Zhao C, Hirata K, Kokubu K, Nagano M, Shinoda K (2007) Anti-human placental antigen complex X-P2 (hPAX-P2) antiserum recognizes C-terminus of huntingtin-associated protein 1A common to 1B as a determinant marker for the stigmoid body. Histochem Cell Biol 128:335–348
Fujinaga R, Takeshita Y, Uozumi K, Yanai A, Yoshioka K, Kokubu K, Shinoda K (2009) Microtubule-dependent formation of the stigmoid body as a cytoplasmic inclusion distinct from pathological aggresomes. Histochem Cell Biol 132:305–318
Fukuhara S, Sakurai A, Sano H, Yamagishi A, Somekawa S, Takakura N, Saito Y, Kangawa K, Mochizuki N (2005) Cyclic AMP potentiates vascular endothelial cadherin-mediated cell-cell contact to enhance endothelial barrier function through an Epac-Rap1 signaling pathway. Mol Cell Biol 25:136–146
Fulka H, Novakova Z, Mosko T, Fulka J Jr (2009) The inability of fully grown germinal vesicle stage oocyte cytoplasm to transcriptionally silence transferred transcribing nuclei. Histochem Cell Biol 132(4):457–468
Gallieni M, Cozzolino M, Fallabrino G, Pasho S, Olivi L, Brancaccio D (2009) Vitamin D: physiology and pathophysiology. Int J Artif Organs 32:87–94
Ghajar CM, Bissell MJ (2008) Extracellular matrix control of mammary gland morphogenesis and tumorigenesis: insights from imaging. Histochem Cell Biol 130:1105–1118
Giacomello E, Sorrentino V (2009) Localization of ank1.5 in the sarcoplasmic reticulum precedes that of SERCA and RyR: relationship with the organization of obscurin in developing sarcomeres. Histochem Cell Biol 131:371–382
Giepmans BN (2008) Bridging fluorescence microscopy and electron microscopy. Histochem Cell Biol 130:211–217

Goldwich A, Baulmann DC, Ohlmann A, Flugel-Koch C, Schocklmann H, Tamm ER (2005) Myocilin is expressed in the glomerulus of the kidney and induced in mesangioproliferative glomerulonephritis. Kidney Int 67:140–151

Goldwich A, Scholz M, Tamm ER (2009) Myocilin promotes substrate adhesion, spreading and formation of focal contacts in podocytes and mesangial cells. Histochem Cell Biol 131:167–180

Gotow T, Shiozaki M, Higashi T, Yoshimura K, Shibata M, Kominami E, Uchiyama Y (2008) Hepatic gap junctions in the hepatocarcinogen-resistant DRH rat. Histochem Cell Biol 130:583–594

Gramann M, Wendler O, Haeberle L, Schick B (2009) Prominent collagen type VI expression in juvenile angiofibromas. Histochem Cell Biol 131:155–164

Groom AC, Schmidt EE, MacDonald IC (1991) Microcirculatory pathways and blood flow in spleen: new insights from washout kinetics, corrosion casts, and quantitative intravital videomicroscopy. Scanning Microsc 5:159–173; discussion 173–154

Guarino M, Tosoni A, Nebuloni M (2009) Direct contribution of epithelium to organ fibrosis: epithelial-mesenchymal transition. Hum Pathol 40:1365–1376

Gubhaju L, Laslett A, Bertram JF, Zulli A, Black MJ (2008) Immunohistochemical localisation of TRA-1–60, TRA-1–81, GCTM-2 and podocalyxin in the developing baboon kidney. Histochem Cell Biol 129:651–657

Guo W, Sun J, Xu X, Bunstock G, He C, Xiang Z (2009) P2X receptors are differentially expressed on vasopressin- and oxytocin-containing neurons in the supraoptic and paraventricular nuclei of rat hypothalamus. Histochem Cell Biol 131:29–41

Gurke S, Barroso JF, Gerdes HH (2008) The art of cellular communication: tunneling nanotubes bridge the divide. Histochem Cell Biol 129:539–550

Hansen GH, Rasmussen K, Niels-Christiansen LL, Danielsen EM (2009) Lipopolysaccharide-binding protein: localization in secretory granules of Paneth cells in the mouse small intestine. Histochem Cell Biol 131:727–732

Harada M, Kenmotsu S, Nakasone N, Nakakura-Ohshima K, Ohshima H (2008) Cell dynamics in the pulpal healing process following cavity preparation in rat molars. Histochem Cell Biol 130:773–783

Harada Y, Dai P, Yamaoka Y, Ogawa M, Tanaka H, Nosaka K, Akaji K, Takamatsu T (2009) Intracellular dynamics of topoisomerase I inhibitor, CPT-11, by slit-scanning confocal Raman microscopy. Histochem Cell Biol 132:39–46

Hasan SS, Ashraf GM, Banu N (2007) Galectins—potential targets for cancer therapy. Cancer Lett 253:25–33

Hasegawa T, Matsuzaki T, Tajika Y, Ablimit A, Suzuki T, Aoki T, Hagiwara H, Takata K (2007) Differential localization of aquaporin-2 and glucose transporter 4 in polarized MDCK cells. Histochem Cell Biol 127:233–241

Hayman AR, Macary P, Lehner PJ, Cox TM (2001) Tartrate-resistant acid phosphatase (Acp 5): identification in diverse human tissues and dendritic cells. J Histochem Cytochem 49:675–684

He W, Cowin P, Stokes DL (2003) Untangling desmosomal knots with electron tomography. Science 302:109–113

Hengartner MO (2000) The biochemistry of apoptosis. Nature 407:770–776

Hentschke M, Hentschke S, Borgmeyer U, Hubner CA, Kurth I (2009) The murine AE4 promoter predominantly drives type B intercalated cell specific transcription. Histochem Cell Biol 132(4):405–412

Hirano K, Guhl B, Roth J, Ziak M (2009) A cell culture system for the induction of Mallory bodies: Mallory bodies and aggresomes represent different types of inclusion bodies. Histochem Cell Biol 132:293–304

Hollander GA, Peterson P (2009) Learning to be tolerant: how T cells keep out of trouble. J Intern Med 265:541–561

Hosoya A, Lee JM, Cho SW, Kim JY, Shinozaki N, Shibahara T, Shimono M, Jung HS (2008) Morphological evidence of basal keratinocyte migration during the re-epithelialization process. Histochem Cell Biol 130:1165–1175

Hubner S, Jans DA, Drenckhahn D (2001) Roles of cytoskeletal and junctional plaque proteins in nuclear signaling. Int Rev Cytol 208:207–265

Hughes H, Stephens DJ (2008) Assembly, organization, and function of the COPII coat. Histochem Cell Biol 129:129–151

Huizinga JD, Thuneberg L, Kluppel M, Malysz J, Mikkelsen HB, Bernstein A (1995) W/kit gene required for interstitial cells of Cajal and for intestinal pacemaker activity. Nature 373:347–349

Iborra FJ, Buckle V (2008) Wide confocal cytometry: a new approach to study proteomic and structural changes in the cell nucleus during the cell cycle. Histochem Cell Biol 129:45–53

Iino S, Horiguchi K, Horiguchi S, Nojyo Y (2009) c-Kit-negative fibroblast-like cells express platelet-derived growth factor receptor alpha in the murine gastrointestinal musculature. Histochem Cell Biol 131:691–702

Inai T, Sengoku A, Hirose E, Iida H, Shibata Y (2008) Comparative characterization of mouse rectum CMT93-I and -II cells by expression of claudin isoforms and tight junction morphology and function. Histochem Cell Biol 129:223–232

Inai T, Sengoku A, Hirose E, Iida H, Shibata Y (2009) Freeze-fracture electron microscopic study of tight junction strands in HEK293 cells and MDCK II cells expressing claudin-1 mutants in the second extracellular loop. Histochem Cell Biol 131:681–690

Jaeger K, Paulsen F, Wohlrab J (2008) Characterization of cationic amino acid transporters (hCATs) 1 and 2 in human skin. Histochem Cell Biol 129:321–329

Jaszai J, Fargeas CA, Haase M, Farkas LM, Huttner WB, Corbeil D (2008) Robust expression of Prominin-2 all along the adult male reproductive system and urinary bladder. Histochem Cell Biol 130:749–759

Jeschke U, Mylonas I, Kunert-Keil C, Stahn R, Scholz C, Janni W, Kuhn C, Schroder E, Mayr D, Friese K (2009) Immunohistochemistry, glycosylation and immunosuppression of glycodelin in human ovarian cancer. Histochem Cell Biol 131:283–295

Jirikowski GF, Kauntzer UW, Dief Ael E, Caldwell JD (2009) Distribution of vitamin D binding protein expressing neurons in the rat hypothalamus. Histochem Cell Biol 131:365–370

Jocken JW, Smit E, Goossens GH, Essers YP, van Baak MA, Mensink M, Saris WH, Blaak EE (2008) Adipose triglyceride lipase (ATGL) expression in human skeletal muscle is type I (oxidative) fiber specific. Histochem Cell Biol 129:535–538

Jones SE, Jomary C (2002) Clusterin. Int J Biochem Cell Biol 34:427–431

Jun H, Song Z, Chen W, Zanhua R, Yonghong S, Shuxia L, Huijun D (2009) In vivo and in vitro effects of SREBP-1 on diabetic renal tubular lipid accumulation and RNAi-mediated gene silencing study. Histochem Cell Biol 131:327–345

Kahle M, Pridalova J, Spacek M, Dzijak R, Hozak P (2007) Nuclear myosin is ubiquitously expressed and evolutionary conserved in vertebrates. Histochem Cell Biol 127:139–148

Kajiya H, Takekoshi S, Takei M, Egashira N, Miyakoshi T, Serizawa A, Teramoto A, Osamura RY (2009) Selection of buffer pH by the isoelectric point of the antigen for the efficient heat-induced epitope retrieval: re-appraisal for nuclear protein pathobiology. Histochem Cell Biol (in press)

Kalbe C, Mau M, Wollenhaupt K, Rehfeldt C (2007) Evidence for estrogen receptor alpha and beta expression in skeletal muscle of pigs. Histochem Cell Biol 127:95–107

Kaneko Y, Lecce L, Murphy CR (2009) Ovarian hormones regulate expression of the focal adhesion proteins, talin and paxillin, in rat uterine luminal but not glandular epithelial cells. Histochem Cell Biol (in press)

Karaoz E, Aksoy A, Ayhan S, Sariboyaci AE, Kaymaz F, Kasap M (2009) Characterization of mesenchymal stem cells from rat bone marrow: ultrastructural properties, differentiation potential and immunophenotypic markers. Histochem Cell Biol 132(5):533–546

Karnati S, Baumgart-Vogt E (2008) Peroxisomes in mouse and human lung: their involvement in pulmonary lipid metabolism. Histochem Cell Biol 130:719–740

Karnati S, Baumgart-Vogt E (2009) Peroxisomes in airway epithelia and future prospects of these organelles for pulmonary cell biology. Histochem Cell Biol 131:447–454

Keattikunpairoj S, Wakayama T, Yamamoto M, Nakaya MA, Nakata H, Hipkaeo W, Sakulsak N, Iseki S (2009) Expression of cAMP response element-binding protein in the duct system of the mouse submandibular gland. Histochem Cell Biol (in press)

Kestler C, Neuhuber WL, Raab M (2009) Distribution of P2X(3) receptor immunoreactivity in myenteric ganglia of the mouse esophagus. Histochem Cell Biol 131:13–27

Kim JI, Young GD, Jin L, Somlyo AV, Eto M (2009a) Expression of CPI-17 in smooth muscle during embryonic development and in neointimal lesion formation. Histochem Cell Biol 132:191–198

Kim JS, Song MS, Seo HS, Yang M, Kim SH, Kim JC, Kim H, Saito TR, Shin T, Moon C (2009b) Immunohistochemical analysis of cAMP response element-binding protein in mouse testis during postnatal development and spermatogenesis. Histochem Cell Biol 131:501–507

Kim RH, Takabe K, Milstien S, Spiegel S (2009c) Export and functions of sphingosine-1-phosphate. Biochim Biophys Acta 1791:692–696

Kirat D, Kato S (2009) Monocarboxylate transporter genes in the mammary gland of lactating cows. Histochem Cell Biol 132(4):447–455

Kobus K, Nazari EM, Muller YM (2009) Effects of folic acid and homocysteine on spinal cord morphology of the chicken embryo. Histochem Cell Biol 132(5):525–532

Kojic S, Medeot E, Guccione E, Krmac H, Zara I, Martinelli V, Valle G, Faulkner G (2004) The Ankrd2 protein, a link between the sarcomere and the nucleus in skeletal muscle. J Mol Biol 339:313–325

Kolling GL, Obata F, Gross LK, Obrig TG (2008) Immunohistologic techniques for detecting the glycolipid Gb(3) in the mouse kidney and nervous system. Histochem Cell Biol 130:157–164

Kredy-Farhan L, Kotev-Emeth S, Savion N (2008) Involvement of cortactin and phosphotyrosine proteins in cell-cell contact formation in cultured bovine corneal endothelial cells. Histochem Cell Biol 129:193–202

Kress M, Karasek J, Ferrer-Montiel AV, Scherbakov N, Haberberger RV (2008) TRPC channels and diacylglycerol dependent calcium signaling in rat sensory neurons. Histochem Cell Biol 130:655–667

Kunert-Keil C, Jeschke U, Simms G, Kasper M (2009) Increased expression of glycodelin mRNA and protein in rat lungs during ovalbumin-induced allergic airway inflammation. Histochem Cell Biol 131:383–390

Kurz T, Terman A, Gustafsson B, Brunk UT (2008) Lysosomes in iron metabolism, ageing and apoptosis. Histochem Cell Biol 129:389–406

Kwon TH, Nielsen J, Moller HB, Fenton RA, Nielsen S, Frokiaer J (2009) Aquaporins in the kidney. Handb Exp Pharmacol (190):95–132

La Rocca G, Anzalone R, Corrao S, Magno F, Loria T, Lo Iacono M, Di Stefano A, Giannuzzi P, Marasa L, Cappello F, Zummo G, Farina F (2009) Isolation and characterization of Oct-4+/HLA-G+ mesenchymal stem cells from human umbilical cord matrix: differentiation potential and detection of new markers. Histochem Cell Biol 131:267–282

Lang P, Lange S, Delbro D, Andersson G (2009) Induction and cellular expression of tartrate resistant acid phosphatase during dextran sodium sulphate induced colitis in rats. Histochem Cell Biol (in press)

Lange F, Brandt B, Tiedge M, Jonas L, Jeschke U, Pohland R, Walzel H (2009) Galectin-1 induced activation of the mitochondrial apoptotic pathway: evidence for a connection between death-receptor and mitochondrial pathways in human Jurkat T lymphocytes. Histochem Cell Biol 132:211–223

Larsson LI, Bjerregaard B, Wulf-Andersen L, Talts JF (2007) Syncytin and cancer cell fusions. Sci World J 7:1193–1197

Larsson LI, Bjerregaard B, Talts JF (2008) Cell fusions in mammals. Histochem Cell Biol 129:551–561

Lavoie C, Paiement J (2008) Topology of molecular machines of the endoplasmic reticulum: a compilation of proteomics and cytological data. Histochem Cell Biol 129:117–128

Le Bitoux MA, Stamenkovic I (2008) Tumor-host interactions: the role of inflammation. Histochem Cell Biol 130:1079–1090

Lee MJ, Cai J, Kwak SW, Cho SW, Harada H, Jung HS (2009) MAPK mediates Hsp25 signaling in incisor development. Histochem Cell Biol 131:593–603

Lenie S, Smitz J (2008) Estrogen receptor subtypes localization shifts in cultured mouse ovarian follicles. Histochem Cell Biol 129:827–840

Lenne PF (2009) Probing cell-surface dynamics and mechanics at different scales. Histochem Cell Biol 132:247–252

Lenne PF, Rigneault H, Marguet D, Wenger J (2008) Fluorescence fluctuations analysis in nanoapertures: physical concepts and biological applications. Histochem Cell Biol 130:795–805

Leonardi E, Ciapetti G, Baglio SR, Devescovi V, Baldini N, Granchi D (2009) Osteogenic properties of late adherent subpopulations of human bone marrow stromal cells. Histochem Cell Biol 132(5):547–557

Levy E, Menard D, Delvin E, Montoudis A, Beaulieu JF, Mailhot G, Dube N, Sinnett D, Seidman E, Bendayan M (2009) Localization, function and regulation of the two intestinal fatty acid-binding protein types. Histochem Cell Biol 132:351–367

Libby P, Aikawa M, Jain MK (2006) Vascular endothelium and atherosclerosis. Handb Exp Pharmacol (176 Pt 2):285–306

Lim RY, Fahrenkrog B, Koser J, Schwarz-Herion K, Deng J, Aebi U (2007) Nanomechanical basis of selective gating by the nuclear pore complex. Science 318:640–643

Lim RY, Aebi U, Fahrenkrog B (2008) Towards reconciling structure and function in the nuclear pore complex. Histochem Cell Biol 129:105–116

Lin JJ, Lin JL (1986) Assembly of different isoforms of actin and tropomyosin into the skeletal tropomyosin-enriched microfilaments during differentiation of muscle cells in vitro. J Cell Biol 103:2173–2183

Lindig TM, Kumar V, Kikinis R, Pieper S, Schrodl F, Neuhuber WL, Brehmer A (2009) Spiny versus stubby: 3D reconstruction of human myenteric (type I) neurons. Histochem Cell Biol 131:1–12

Lindstrom M, Thornell LE (2009) New multiple labelling method for improved satellite cell identification in human muscle: application to a cohort of power-lifters and sedentary men. Histochem Cell Biol 132:141–157

Lohr M, Kaltner H, Lensch M, Andre S, Sinowatz F, Gabius HJ (2008) Cell-type-specific expression of murine multifunctional galectin-3 and its association with follicular atresia/luteolysis in contrast to pro-apoptotic galectins-1 and -7. Histochem Cell Biol 130:567–581

Lopez C, Lejeune M, Salvado MT, Escriva P, Bosch R, Pons LE, Alvaro T, Roig J, Cugat X, Baucells J, Jaen J (2008) Automated quantification of nuclear immunohistochemical markers with different complexity. Histochem Cell Biol 129:379–387

Lopez C, Jaen Martinez J, Lejeune M, Escriva P, Salvado MT, Pons LE, Alvaro T, Baucells J, Garcia-Rojo M, Cugat X, Bosch R (2009) Roundness variation in JPEG images affects the automated process of nuclear immunohistochemical quantification: correction with a linear regression model. Histochem Cell Biol 132(4):469–477

Lorusso G, Ruegg C (2008) The tumor microenvironment and its contribution to tumor evolution toward metastasis. Histochem Cell Biol 130:1091–1103

Low M, Sandoval D, Aviles E, Perez F, Nualart F, Henriquez JP (2009) The ascorbic acid transporter SVCT2 is expressed in slow-twitch skeletal muscle fibres. Histochem Cell Biol 131:565–574

Lucic V, Leis A, Baumeister W (2008) Cryo-electron tomography of cells: connecting structure and function. Histochem Cell Biol 130:185–196

Luini A, Mironov AA, Polishchuk EV, Polishchuk RS (2008) Morphogenesis of post-Golgi transport carriers. Histochem Cell Biol 129:153–161

Ma XJ, Fu YY, Li YX, Chen LM, Chai K, Wang YL (2009) Prostasin inhibits cell invasion in human choriocarcinomal JEG-3 cells. Histochem Cell Biol (in press)

Maby-El Hajjami H, Petrova TV (2008) Developmental and pathological lymphangiogenesis: from models to human disease. Histochem Cell Biol 130:1063–1078

Maeda S (2008) Genetics of diabetic nephropathy. Ther Adv Cardiovasc Dis 2:363–371

Majoul IV, Onichtchouk D, Butkevich E, Wenzel D, Chailakhyan LM, Duden R (2009) Limiting transport steps and novel interactions of Connexin-43 along the secretory pathway. Histochem Cell Biol 132:263–280

Makitie LT, Kanerva K, Sankila A, Andersson LC (2009) High expression of antizyme inhibitor 2, an activator of ornithine decarboxylase in steroidogenic cells of human gonads. Histochem Cell Biol (in press)

Makrigiannakis A, Karamouti M, Petsas G, Makris N, Nikas G, Antsaklis A (2009) The expression of receptivity markers in the fallopian tube epithelium. Histochem Cell Biol 132:159–167

Malatesta M, Furlan S, Mariotti R, Zancanaro C, Nobile C (2009) Distribution of the epilepsy-related Lgi1 protein in rat cortical neurons. Histochem Cell Biol 132(5):505–513

Maly IP, Landmann L (2008) Bile duct ligation in the rat causes upregulation of ZO-2 and decreased colocalization of claudins with ZO-1 and occludin. Histochem Cell Biol 129:289–299

Mandell JW (2008) Immunohistochemical assessment of protein phosphorylation state: the dream and the reality. Histochem Cell Biol 130:465–471

Manning J, Kumar S (2007) NEDD1: function in microtubule nucleation, spindle assembly and beyond. Int J Biochem Cell Biol 39:7–11

Manning JA, Colussi PA, Koblar SA, Kumar S (2008) Nedd1 expression as a marker of dynamic centrosomal localization during mouse embryonic development. Histochem Cell Biol 129:751–764

Mansuroglu T, Dudas J, Elmaouhoub A, Joza TZ, Ramadori G (2009) Hepatoblast and mesenchymal cell-specific gene-expression in fetal rat liver and in cultured fetal rat liver cells. Histochem Cell Biol 132:11–19

Marini M, Falcieri E, Margonato V, Trere D, Lapalombella R, di Tullio S, Marchionni C, Burattini S, Samaja M, Esposito F, Veicsteinas A (2008) Partial persistence of exercise-induced myocardial angiogenesis following 4-week detraining in the rat. Histochem Cell Biol 129:479–487

Marks DL, Bittman R, Pagano RE (2008) Use of Bodipy-labeled sphingolipid and cholesterol analogs to examine membrane microdomains in cells. Histochem Cell Biol 130:819–832

Martin-Satue M, Lavoie EG, Pelletier J, Fausther M, Csizmadia E, Guckelberger O, Robson SC, Sevigny J (2009) Localization of plasma membrane bound NTPDases in the murine reproductive tract. Histochem Cell Biol 131:615–628

Maya-Monteiro CM, Bozza PT (2008) Leptin and mTOR: partners in metabolism and inflammation. Cell Cycle 7:1713–1717

Mayhew TM, Lucocq JM (2008a) Developments in cell biology for quantitative immunoelectron microscopy based on thin sections: a review. Histochem Cell Biol 130:299–313

Mayhew TM, Lucocq JM (2008b) Quantifying immunogold labelling patterns of cellular compartments when they comprise mixtures of membranes (surface-occupying) and organelles (volume-occupying). Histochem Cell Biol 129:367–378

Mehlmann LM (2005) Stops and starts in mammalian oocytes: recent advances in understanding the regulation of meiotic arrest and oocyte maturation. Reproduction 130:791–799

Mei F, Zhu J, Guo S, Zhou DS, Han J, Yu B, Li SF, Jiang ZY, Xiong CJ (2009) An age-dependent proliferation is involved in the postnatal development of interstitial cells of Cajal in the small intestine of mice. Histochem Cell Biol 131:43–53

Meiblitzer-Ruppitsch C, Vetterlein M, Stangl H, Maier S, Neumuller J, Freissmuth M, Pavelka M, Ellinger A (2008) Electron microscopic visualization of fluorescent signals in cellular compartments and organelles by means of DAB-photoconversion. Histochem Cell Biol 130:407–419

Merg A, Howe JR (2004) Genetic conditions associated with intestinal juvenile polyps. Am J Med Genet C Semin Med Genet 129C:44–55

Michelucci R, Pasini E, Nobile C (2009) Lateral temporal lobe epilepsies: clinical and genetic features. Epilepsia 50(Suppl 5):52–54

Mikkelsen HB, Larsen JO, Hadberg H (2008) The macrophage system in the intestinal muscularis externa during inflammation: an immunohistochemical and quantitative study of osteopetrotic mice. Histochem Cell Biol 130:363–373

Milicevic NM, Nohroudi K, Labudovic-Borovic M, Milicevic Z, Pfeffer K, Westermann J (2006) Metallophilic macrophages are lacking in the thymus of lymphotoxin-beta receptor-deficient mice. Histochem Cell Biol 126:687–693

Milicevic NM, Milicevic Z, Miljkovic MD, Labudovic-Borovic M, Laan M, Peterson P, Kisand K, Scott HS, Qu N, Westermann J (2009) Metallophilic macrophages are fully developed in the thymus of autoimmune regulator (Aire)-deficient mice. Histochem Cell Biol 131:643–649

Mingle LA, Bonamy G, Barroso M, Liao G, Liu G (2009) LPA-induced mutually exclusive subcellular localization of active RhoA and Arp2 mRNA revealed by sequential FRET and FISH. Histochem Cell Biol 132:47–58

Misteli T (2008) Physiological importance of RNA and protein mobility in the cell nucleus. Histochem Cell Biol 129:5–11

Mittapalli VR, Christ B, Prols F, Scaal M (2009) Pleiotrophin is expressed in avian somites and tendon anlagen. Histochem Cell Biol 132(4):413–422

Mizuno Y, Suzuki M, Nakagawa H, Ninagawa N, Torihashi S (2009) Switching of actin isoforms in skeletal muscle differentiation using mouse ES cells. Histochem Cell Biol (in press)

Moll R, Divo M, Langbein L (2008) The human keratins: biology and pathology. Histochem Cell Biol 129:705–733

Moller LN, Stidsen CE, Hartmann B, Holst JJ (2003) Somatostatin receptors. Biochim Biophys Acta 1616:1–84

Morrison EE, Costanzo RM (1992) Morphology of olfactory epithelium in humans and other vertebrates. Microsc Res Tech 23:49–61

Mulvey MA, Lopez-Boado YS, Wilson CL, Roth R, Parks WC, Heuser J, Hultgren SJ (1998) Induction and evasion of host defenses by type 1-piliated uropathogenic *Escherichia coli*. Science 282:1494–1497

Nabeshima K, Iwasaki H, Koga K, Hojo H, Suzumiya J, Kikuchi M (2006) Emmprin (basigin/CD147): matrix metalloproteinase modulator and multifunctional cell recognition molecule that plays a critical role in cancer progression. Pathol Int 56:359–367

Nakakura T, Sato M, Suzuki M, Hatano O, Takemori H, Taniguchi Y, Minoshima Y, Tanaka S (2009) The spatial and temporal expression of delta-like protein 1 in the rat pituitary gland during development. Histochem Cell Biol 131:141–153

Nakatsuka T, Gu JG (2006) P2X purinoceptors and sensory transmission. Pflugers Arch 452:598–607

Naz S, Giguere CM, Kohrman DC, Mitchem KL, Riazuddin S, Morell RJ, Ramesh A, Srisailpathy S, Deshmukh D, Griffith AJ, Friedman TB, Smith RJ, Wilcox ER (2002) Mutations in a novel gene, TMIE, are associated with hearing loss linked to the DFNB6 locus. Am J Hum Genet 71:632–636

Nestorovic N, Manojlovic-Stojanoski M, Ristic N, Sekulic M, Sosic-Jurjevic B, Filipovic B, Milosevic V (2008) Somatostatin-14 influences pituitary-ovarian axis in peripubertal rats. Histochem Cell Biol 130:699–708

Nitschke C, Garin A, Kosco-Vilbois M, Gunzer M (2008) 3D and 4D imaging of immune cells in vitro and in vivo. Histochem Cell Biol 130:1053–1062

Nueda ML, Baladron V, Garcia-Ramirez JJ, Sanchez-Solana B, Ruvira MD, Rivero S, Ballesteros MA, Monsalve EM, Diaz-Guerra MJ, Ruiz-Hidalgo MJ, Laborda J (2007) The novel gene EGFL9/Dlk2, highly homologous to Dlk1, functions as a modulator of adipogenesis. J Mol Biol 367:1270–1280

O'Leary TJ, Fowler CB, Evers DL, Mason JT (2009) Protein fixation and antigen retrieval: chemical studies. Biotech Histochem 84:217–221

Ohama Y, Hayashi K (2009) Relocalization of a microtubule-anchoring protein, ninein, from the centrosome to dendrites during differentiation of mouse neurons. Histochem Cell Biol 132(5):515–524

Omary MB (2009) "IF-pathies": a broad spectrum of intermediate filament-associated diseases. J Clin Invest 119:1756–1762

Ono T (2005) Studies of the FABP family: a retrospective. Mol Cell Biochem 277:1–6

Orlowski D, Bjarkam CR (2009) Autometallographic enhancement of the Golgi-Cox staining enables high resolution visualization of dendrites and spines. Histochem Cell Biol 132:369–374

Osten L, Kubitza M, Gallagher AR, Kastner J, Olbrich H, de Vries U, Kees F, Lelongt B, Somlo S, Omran H, Witzgall R (2009) Doxycycline accelerates renal cyst growth and fibrosis in the pcy/pcy mouse model of type 3 nephronophthisis, a form of recessive polycystic kidney disease. Histochem Cell Biol 132:199–210

Panasophonkul S, Apisawetakan S, Cummins SF, York PS, Degnan BM, Hanna PJ, Saitongdee P, Sobhon P, Sretarugsa P (2009) Molecular characterization and analysis of a truncated serotonin receptor gene expressed in neural and reproductive tissues of abalone. Histochem Cell Biol 131:629–642

Pavelka M, Neumuller J, Ellinger A (2008) Retrograde traffic in the biosynthetic-secretory route. Histochem Cell Biol 129:277–288

Pavlakis E, Makrygiannis AK, Chiotaki R, Chalepakis G (2008) Differential localization profile of Fras1/Frem proteins in epithelial basement membranes of newborn and adult mice. Histochem Cell Biol 130:785–793

Pegg AE (2006) Regulation of ornithine decarboxylase. J Biol Chem 281:14529–14532

Petri S, Krampfl K, Kuhlemann K, Dengler R, Grothe C (2009) Preserved expression of fibroblast growth factor (FGF)-2 and FGF receptor 1 in brain and spinal cord of amyotrophic lateral sclerosis patients. Histochem Cell Biol 131:509–519

Picard N, Baum O, Vogetseder A, Kaissling B, Le Hir M (2008) Origin of renal myofibroblasts in the model of unilateral ureter obstruction in the rat. Histochem Cell Biol 130:141–155

Pierson J, Sani M, Tomova C, Godsave S, Peters PJ (2009) Toward visualization of nanomachines in their native cellular environment. Histochem Cell Biol 132:253–262

Poole RC, Halestrap AP (1993) Transport of lactate and other monocarboxylates across mammalian plasma membranes. Am J Physiol 264:C761–C782

Prochnow N, Dermietzel R (2008) Connexons and cell adhesion: a romantic phase. Histochem Cell Biol 130:71–77

Publicover SJ, Giojalas LC, Teves ME, de Oliveira GS, Garcia AA, Barratt CL, Harper CV (2008) Ca^{2+} signalling in the control of motility and guidance in mammalian sperm. Front Biosci 13:5623–5637

Ratajska A, Czarnowska E, Kolodzinska A, Jablonska A, Stachurska E (2009) New morphological aspects of blood islands formation in the embryonic mouse hearts. Histochem Cell Biol 131:297–311

Renegar RH, Chalovich JM, Leinweber BD, Zary JT, Schroeter MM (2009) Localization of the actin-binding protein fesselin in chicken smooth muscle. Histochem Cell Biol 131:191–196

Reupke T, Puschel B, Viebahn C (2009) Tracing and ablation of single cells in the mammalian blastocyst using fluorescent DNA staining and multi-photon laser microscopy. Histochem Cell Biol 131:521–530

Robinson JM (2008) Reactive oxygen species in phagocytic leukocytes. Histochem Cell Biol 130:281–297

Robinson JM (2009) Phagocytic leukocytes and reactive oxygen species. Histochem Cell Biol 131:465–469

Rocha T, de Souza BM, Palma MS, da Cruz-Hofling MA, Harris JB (2009) The neurotoxicological effects of mastoparan Polybia-MPII at the murine neuromuscular junction: an ultrastructural and immunocytochemical study. Histochem Cell Biol 132(4):395–404

Roediger B, Ng LG, Smith AL, de St Groth BF, Weninger W (2008) Visualizing dendritic cell migration within the skin. Histochem Cell Biol 130:1131–1146

Roepstorff K, Grovdal L, Grandal M, Lerdrup M, van Deurs B (2008) Endocytic downregulation of ErbB receptors: mechanisms and relevance in cancer. Histochem Cell Biol 129:563–578

Roingeard P, Hourioux C, Blanchard E, Prensier G (2008) Hepatitis C virus budding at lipid droplet-associated ER membrane visualized by 3D electron microscopy. Histochem Cell Biol 130:561–566

Rosenzweig A, Seidman CE (1991) Atrial natriuretic factor and related peptide hormones. Annu Rev Biochem 60:229–255

Rosicarelli B, Stefanini S (2009) DEHP effects on histology and cell proliferation in lung of newborn rats. Histochem Cell Biol 131:491–500

Roth J (1996) The silver anniversary of gold: 25 years of the colloidal gold marker system for immunocytochemistry and histochemistry. Histochem Cell Biol 106:1–8

Roth J, Fahimi HD, Drenckhahn D (2008a) Celebration of the 50th anniversary of publication of Histochemistry and Cell Biology. Histochem Cell Biol 129:1–3

Roth J, Yam GH, Fan J, Hirano K, Gaplovska-Kysela K, Le Fourn V, Guhl B, Santimaria R, Torossi T, Ziak M, Zuber C (2008b) Protein quality control: the who's who, the where's and therapeutic escapes. Histochem Cell Biol 129:163–177

Rudini N, Dejana E (2008) Adherens junctions. Curr Biol 18:R1080–R1082

Rustom A (2009) Hen or egg?: some thoughts on tunneling nanotubes. Ann N Y Acad Sci 1178:129–136

Ruttinger C, Bergmann M, Fink L, Pesch S, Seitz K, Trautmann A, Steger K, Konrad L, Brehm R (2008) Expression of connexin 43 in normal canine testes and canine testicular tumors. Histochem Cell Biol 130:537–548

Saftig P, Klumperman J (2009) Lysosome biogenesis and lysosomal membrane proteins: trafficking meets function. Nat Rev Mol Cell Biol 10:623–635

Salanova M, Schiffl G, Rittweger J, Felsenberg D, Blottner D (2008) Ryanodine receptor type-1 (RyR1) expression and protein S-nitrosylation pattern in human soleus myofibres following bed rest and exercise countermeasure. Histochem Cell Biol 130:105–118

Salanova M, Schiffl G, Blottner D (2009) Atypical fast SERCA1a protein expression in slow myofibers and differential S-nitrosylation prevented by exercise during long term bed rest. Histochem Cell Biol 132(4):383–394

Sandvig K, Torgersen ML, Raa HA, van Deurs B (2008) Clathrin-independent endocytosis: from nonexisting to an extreme degree of complexity. Histochem Cell Biol 129:267–276

Sango K, Yanagisawa H, Takaku S (2007) Expression and histochemical localization of ciliary neurotrophic factor in cultured adult rat dorsal root ganglion neurons. Histochem Cell Biol 128:35–43

Sango K, Yanagisawa H, Komuta Y, Si Y, Kawano H (2008) Neuroprotective properties of ciliary neurotrophic factor for cultured adult rat dorsal root ganglion neurons. Histochem Cell Biol 130:669–679

Sant'Anna C, Parussini F, Lourenco D, de Souza W, Cazzulo JJ, Cunha-e-Silva NL (2008) All Trypanosoma cruzi developmental forms present lysosome-related organelles. Histochem Cell Biol 130:1187–1198

Satir P, Christensen ST (2008) Structure and function of mammalian cilia. Histochem Cell Biol 129:687–693

Sato S, Tsuchiya M, Komaki K, Kusunoki S, Tsuchiya S, Haruyama N, Takahashi I, Sasano Y, Watanabe M (2009) Synthesis and intracellular transportation of type I procollagen during functional differentiation of odontoblasts. Histochem Cell Biol 131:583–591

Schatten H (2008) The mammalian centrosome and its functional significance. Histochem Cell Biol 129:667–686

Schilling K, Oberdick J, Rossi F, Baader SL (2008) Besides Purkinje cells and granule neurons: an appraisal of the cell biology of the interneurons of the cerebellar cortex. Histochem Cell Biol 130:601–615

Schleicher M, Jockusch BM (2008) Actin: its cumbersome pilgrimage through cellular compartments. Histochem Cell Biol 129:695–704

Schmidt T, Fischer S, Tsikolia N, Navarrete Santos A, Rohrbach S, Ramin N, Thieme R, Fischer B (2008) Expression of adipokines in preimplantation rabbit and mice embryos. Histochem Cell Biol 129:817–825

Schormann W, Hammersen FJ, Brulport M, Hermes M, Bauer A, Rudolph C, Schug M, Lehmann T, Nussler A, Ungefroren H, Hutchinson J, Fandrich F, Petersen J, Wursthorn K, Burda MR, Brustle O, Krishnamurthi K, von Mach M, Hengstler JG (2008) Tracking of human cells in mice. Histochem Cell Biol 130:329–338

Schrader M (2009) Anniversaries, peroxisomes and reactive oxygen species. Histochem Cell Biol 131:435–436

Schrader M, Fahimi HD (2008) The peroxisome: still a mysterious organelle. Histochem Cell Biol 129:421–440

Schulze-Tanzil G, Muller RD, Kohl B, Schneider N, Ertel W, Ipaktchi K, Hunigen H, Gemeinhardt O, Stark R, John T (2009) Differing in vitro biology of equine, ovine, porcine and human articular chondrocytes derived from the knee joint: an immunomorphological study. Histochem Cell Biol 131:219–229

Schumann RR, Leong SR, Flaggs GW, Gray PW, Wright SD, Mathison JC, Tobias PS, Ulevitch RJ (1990) Structure and function of lipopolysaccharide binding protein. Science 249:1429–1431

Sebastian S, Settleman J, Reshkin SJ, Azzariti A, Bellizzi A, Paradiso A (2006) The complexity of targeting EGFR signalling in cancer: from expression to turnover. Biochim Biophys Acta 1766:120–139

Semenza GL (2007) Vasculogenesis, angiogenesis, and arteriogenesis: mechanisms of blood vessel formation and remodeling. J Cell Biochem 102:840–847

Sengoku A, Inai T, Shibata Y (2008) Formation of aberrant TJ strands by overexpression of claudin-15 in MDCK II cells. Histochem Cell Biol 129:211–222

Seppala M (1999) Glycodelins: biological activity in reproduction and differentiation. Curr Opin Obstet Gynecol 11:261–263

Shaw CS, Jones DA, Wagenmakers AJ (2008) Network distribution of mitochondria and lipid droplets in human muscle fibres. Histochem Cell Biol 129:65–72

Shaw CS, Sherlock M, Stewart PM, Wagenmakers AJ (2009) Adipophilin distribution and colocalization with lipid droplets in skeletal muscle. Histochem Cell Biol 131:575–581

Shimohira D, Kido MA, Danjo A, Takao T, Wang B, Zhang JQ, Yamaza T, Masuko S, Goto M, Tanaka T (2009) TRPV2 expression in rat oral mucosa. Histochem Cell Biol 132(4):423–433

Shin M, Nakamuta H, Oda-Ueda N, Larsson LI, Fujiwara K (2008a) Immunocytochemical demonstration of polyamines in nucleoli and nuclei. Histochem Cell Biol 129:659–665

Shin SS, Martino JJ, Chen S (2008b) Metabotropic glutamate receptors (mGlus) and cellular transformation. Neuropharmacology 55:396–402

Shlomai J (2004) The structure and replication of kinetoplast DNA. Curr Mol Med 4:623–647

Short K, Wiradjaja F, Smyth I (2007) Let's stick together: the role of the Fras1 and Frem proteins in epidermal adhesion. IUBMB Life 59:427–435

Singhvi A, Garriga G (2009) Asymmetric divisions, aggresomes and apoptosis. Trends Cell Biol 19:1–7

Sirri V, Urcuqui-Inchima S, Roussel P, Hernandez-Verdun D (2008) Nucleolus: the fascinating nuclear body. Histochem Cell Biol 129:13–31

Smith SM, Whitelock JM, Iozzo RV, Little CB, Melrose J (2009) Topographical variation in the distributions of versican, aggrecan and perlecan in the foetal human spine reflects their diverse functional roles in spinal development. Histochem Cell Biol 132(5):491–503

Soldani C, Croce AC, Bottone MG, Fraschini A, Biggiogera M, Bottiroli G, Pellicciari C (2007) Apoptosis in tumour cells photosensitized with Rose Bengal acetate is induced by multiple organelle photodamage. Histochem Cell Biol 128:485–495

Solder E, Kremser C, Rohr I, Hutzler P, Debbage P (2009) Molecular mapping deep within a living human organ: analysis of microvessel function on the timescale of seconds and with sub-micrometre spatial resolution. Histochem Cell Biol 131:537–551

Son S, Kojima T, Decaens C, Yamaguchi H, Ito T, Imamura M, Murata M, Tanaka S, Chiba H, Hirata K, Sawada N (2009) Knockdown of tight junction protein claudin-2 prevents bile canalicular formation in WIF-B9 cells. Histochem Cell Biol 131:411–424

Sorokin SP, Hoyt RF Jr, Shaffer MJ (1997) Ontogeny of neuroepithelial bodies: correlations with mitogenesis and innervation. Microsc Res Tech 37:43–61

Steffl M, Schweiger M, Mayer J, Amselgruber WM (2009) Expression and localization of growth hormone receptor in the oviduct of cyclic and pregnant pigs and mid-implantation conceptuses. Histochem Cell Biol 131:773–779

Steinke A, Meier-Stiegen S, Drenckhahn D, Asan E (2008) Molecular composition of tight and adherens junctions in the rat olfactory epithelium and fila. Histochem Cell Biol 130:339–361

Stemmer A, Beck M, Fiolka R (2008) Widefield fluorescence microscopy with extended resolution. Histochem Cell Biol 130:807–817

Stepulak A, Luksch H, Gebhardt C, Uckermann O, Marzahn J, Sifringer M, Rzeski W, Staufner C, Brocke KS, Turski L, Ikonomidou C (2009) Expression of glutamate receptor subunits in human cancers. Histochem Cell Biol 132(4):435–445

Stewart CL, Roux KJ, Burke B (2007) Blurring the boundary: the nuclear envelope extends its reach. Science 318:1408–1412

Stradalova V, Gaplovska-Kysela K, Hozak P (2008) Ultrastructural and nuclear antigen preservation after high-pressure freezing/freeze-substitution and low-temperature LR White embedding of HeLa cells. Histochem Cell Biol 130:1047–1052

Strnad P, Stumptner C, Zatloukal K, Denk H (2008) Intermediate filament cytoskeleton of the liver in health and disease. Histochem Cell Biol 129:735–749

Studer D, Humbel BM, Chiquet M (2008) Electron microscopy of high pressure frozen samples: bridging the gap between cellular ultrastructure and atomic resolution. Histochem Cell Biol 130:877–889

Su MC, Yang JJ, Chou MY, Hsin CH, Su CC, Li SY (2008) Expression and localization of Tmie in adult rat cochlea. Histochem Cell Biol 130:119–126

Suda RK, Billings PC, Egan KP, Kim JH, McCarrick-Walmsley R, Glaser DL, Porter DL, Shore EM, Pignolo RJ (2009) Circulating osteogenic precursor cells in heterotopic bone formation. Stem Cells 27:2209–2219

Suzuki R, Nourani MR, Saino-Saito S, Abe H, Nochi T, Kiyono H, Spener F, Kondo H, Owada Y (2009a) Localization of fatty acid binding protein of epidermal type common to dendritic cells and presumptive macrophages in Peyer's patches and epithelial M cells of mouse intestine. Histochem Cell Biol (in press)

Suzuki T, Matsunami T, Hisa Y, Takata K, Takamatsu T, Oyamada M (2009b) Roles of gap junctions in glucose transport from glucose transporter 1-positive to -negative cells in the lateral wall of the rat cochlea. Histochem Cell Biol 131:89–102

Suzuki-Kerr H, Lim JC, Vlajkovic SM, Donaldson PJ (2009) Differential membrane redistribution of P2X receptor isoforms in response to osmotic and hyperglycemic stress in the rat lens. Histochem Cell Biol 131:667–680

Swanbeck G (1992) Urea in the treatment of dry skin. Acta Derm Venereol Suppl 177:7–8

Taatjes DJ, Wadsworth MP, Zaman AK, Schneider DJ, Sobel BE (2007) A novel dual staining method for identification of apoptotic cells reveals a modest apoptotic response in infarcted mouse myocardium. Histochem Cell Biol 128:275–283

Taatjes DJ, Sobel BE, Budd RC (2008a) Morphological and cytochemical determination of cell death by apoptosis. Histochem Cell Biol 129:33–43

Taatjes DJ, Wadsworth MP, Quinn AS, Rand JH, Bovill EG, Sobel BE (2008b) Imaging aspects of cardiovascular disease at the cell and molecular level. Histochem Cell Biol 130:235–245

Tahvanainen E, Tahvanainen P, Kaariainen H, Hockerstedt K (2005) Polycystic liver and kidney diseases. Ann Med 37:546–555

Taildeman J, Perez-Novo CA, Rottiers I, Ferdinande L, Waeytens A, De Colvenaer V, Bachert C, Demetter P, Waelput W, Braet K, Cuvelier CA (2009) Human mast cells express leptin and leptin receptors. Histochem Cell Biol 131:703–711

Takahashi K, Tanabe K, Ohnuki M, Narita M, Ichisaka T, Tomoda K, Yamanaka S (2007) Induction of pluripotent stem cells from adult human fibroblasts by defined factors. Cell 131:861–872

Takata K, Matsuzaki T, Tajika Y, Ablimit A, Hasegawa T (2008) Localization and trafficking of aquaporin 2 in the kidney. Histochem Cell Biol 130:197–209

Takebe K, Nio-Kobayashi J, Takahashi-Iwanaga H, Yajima T, Iwanaga T (2009) Cellular expression of a monocarboxylate transporter (MCT1) in the mammary gland and sebaceous gland of mice. Histochem Cell Biol 131:401–409

Takechi R, Galloway S, Pallebage-Gamarallage MM, Johnsen RD, Mamo JC (2008) Three-dimensional immunofluorescent double labelling using polyclonal antibodies derived from the same species: enterocytic colocalization of chylomicrons with Golgi apparatus. Histochem Cell Biol 129:779–784

Takechi R, Galloway S, Pallebage-Gamarallage M, Wellington C, Johnsen R, Mamo JC (2009) Three-dimensional colocalization analysis of plasma-derived apolipoprotein B with amyloid plaques in APP/PS1 transgenic mice. Histochem Cell Biol 131:661–666

Takeshita Y, Fujinaga R, Zhao C, Yanai A, Shinoda K (2006) Huntingtin-associated protein 1 (HAP1) interacts with androgen receptor (AR) and suppresses SBMA-mutant-AR-induced apoptosis. Hum Mol Genet 15:2298–2312

Takkunen M, Ainola M, Vainionpaa N, Grenman R, Patarroyo M, Garcia de Herreros A, Konttinen YT, Virtanen I (2008) Epithelial-mesenchymal transition downregulates laminin alpha5 chain and upregulates laminin alpha4 chain in oral squamous carcinoma cells. Histochem Cell Biol 130:509–525

Talavera K, Nilius B, Voets T (2008) Neuronal TRP channels: thermometers, pathfinders and life-savers. Trends Neurosci 31:287–295

Talbot K, Ansorge O (2006) Recent advances in the genetics of amyotrophic lateral sclerosis and frontotemporal dementia: common pathways in neurodegenerative disease. Hum Mol Genet 15(Spec No 2):R182–R187

Tamaki T, Uchiyama Y, Okada Y, Tono K, Nitta M, Hoshi A, Akatsuka A (2009a) Anabolic-androgenic steroid does not enhance compensatory muscle hypertrophy but significantly diminish muscle damages in the rat surgical ablation model. Histochem Cell Biol 132:71–81

Tamaki T, Uchiyama Y, Okada Y, Tono K, Nitta M, Hoshi A, Akatsuka A (2009b) Multiple stimulations for muscle-nerve-blood vessel unit in compensatory hypertrophied skeletal muscle of rat surgical ablation model. Histochem Cell Biol 132:59–70

Tamura M, Aizawa R, Hori M, Ozaki H (2009) Progressive renal dysfunction and macrophage infiltration in interstitial fibrosis in an adenine-induced tubulointerstitial nephritis mouse model. Histochem Cell Biol 131:483–490

Tashiro K, Nakamura T, Honjo T (1999) The signal sequence trap method. Methods Enzymol 303:479–495

Tempfer H, Wagner A, Gehwolf R, Lehner C, Tauber M, Resch H, Bauer HC (2009) Perivascular cells of the supraspinatus tendon express both tendon- and stem cell-related markers. Histochem Cell Biol 131:733–741

Ten Dam GB, Yamada S, Kobayashi F, Purushothaman A, van de Westerlo EM, Bulten J, Malmstrom A, Sugahara K, Massuger LF, van Kuppevelt TH (2009) Dermatan sulfate domains defined by the novel antibody GD3A12, in normal tissues and ovarian adenocarcinomas. Histochem Cell Biol 132:117–127

Thiry M, Cheutin T, Lamaye F, Thelen N, Meier UT, O'Donohue MF, Ploton D (2009) Localization of Nopp140 within mammalian cells during interphase and mitosis. Histochem Cell Biol 132:129–140

Thomas T, Thomas TJ (2003) Polyamine metabolism and cancer. J Cell Mol Med 7:113–126

Thomsen L, Robinson TL, Lee JC, Farraway LA, Hughes MJ, Andrews DW, Huizinga JD (1998) Interstitial cells of Cajal generate a rhythmic pacemaker current. Nat Med 4:848–851

Tilki D, Kilic N, Herbst H, Reich O, Seitz M, Lauke H, Stief CG, Ergun S (2008) High level of endostatin in epididymal epithelium: protection against primary malignancies in this organ? Histochem Cell Biol 130:527–535

Timson BF, Bowlin BK, Dudenhoeffer GA, George JB (1985) Fiber number, area, and composition of mouse soleus muscle following enlargement. J Appl Physiol 58:619–624

Tobin DM, Bargmann CI (2004) Invertebrate nociception: behaviors, neurons and molecules. J Neurobiol 61:161–174

Tomarev SI, Nakaya N (2009) Olfactomedin domain-containing proteins: possible mechanisms of action and functions in normal development and pathology. Mol Neurobiol 40:122–138

Toth B, Saadat G, Geller A, Scholz C, Schulze S, Friese K, Jeschke U (2008) Human umbilical vascular endothelial cells express

estrogen receptor beta (ERbeta) and progesterone receptor A (PR-A), but not ERalpha and PR-B. Histochem Cell Biol 130:399–405
Tran H, Tanaka A, Litvinovich SV, Medved LV, Haudenschild CC, Argraves WS (1995) The interaction of fibulin-1 with fibrinogen A potential role in hemostasis and thrombosis. J Biol Chem 270:19458–19464
Trinkle-Mulcahy L, Lamond AI (2007) Toward a high-resolution view of nuclear dynamics. Science 318:1402–1407
Tsikolia N, Merkwitz C, Sass K, Sakurai M, Spanel-Borowski K, Ricken AM (2009) Characterization of bovine fetal Leydig cells by KIT expression. Histochem Cell Biol (in press)
Tsukamoto Y, Hijiya N, Yano S, Yokoyama S, Nakada C, Uchida T, Matsuura K, Moriyama M (2008) Arpp/Ankrd2, a member of the muscle ankyrin repeat proteins (MARPs), translocates from the I-band to the nucleus after muscle injury. Histochem Cell Biol 129:55–64
Turlejski K (1996) Evolutionary ancient roles of serotonin: long-lasting regulation of activity and development. Acta Neurobiol Exp 56:619–636
Uchiyama Y, Shibata M, Koike M, Yoshimura K, Sasaki M (2008) Autophagy-physiology and pathophysiology. Histochem Cell Biol 129:407–420
Uehara K, Uehara A (2008) Localization of claudin-5 and ZO-1 in rat spleen sinus endothelial cells. Histochem Cell Biol 129:95–103
Valdmanis PN, Daoud H, Dion PA, Rouleau GA (2009) Recent advances in the genetics of amyotrophic lateral sclerosis. Curr Neurol Neurosci Rep 9:198–205
Van Rossen E, Vander Borght S, van Grunsven LA, Reynaert H, Bruggeman V, Blomhoff R, Roskams T, Geerts A (2009) Vinculin and cellular retinol-binding protein-1 are markers for quiescent and activated hepatic stellate cells in formalin-fixed paraffin embedded human liver. Histochem Cell Biol 131:313–325
Varela-Moreiras G, Murphy MM, Scott JM (2009) Cobalamin, folic acid, and homocysteine. Nutr Rev 67(Suppl 1):S69–S72
Varoga D, Wruck CJ, Tohidnezhad M, Brandenburg L, Paulsen F, Mentlein R, Seekamp A, Besch L, Pufe T (2009) Osteoblasts participate in the innate immunity of the bone by producing human beta defensin-3. Histochem Cell Biol 131:207–218
Veranic P, Erman A, Kerec-Kos M, Bogataj M, Mrhar A, Jezernik K (2009) Rapid differentiation of superficial urothelial cells after chitosan-induced desquamation. Histochem Cell Biol 131:129–139
Verbrugghe P, Kujala P, Waelput W, Peters PJ, Cuvelier CA (2008) Clusterin in human gut-associated lymphoid tissue, tonsils, and adenoids: localization to M cells and follicular dendritic cells. Histochem Cell Biol 129:311–320
Verveer PJ, Bastiaens PI (2008) Quantitative microscopy and systems biology: seeing the whole picture. Histochem Cell Biol 130:833–843
Vinken M, Vanhaecke T, Papeleu P, Snykers S, Henkens T, Rogiers V (2006) Connexins and their channels in cell growth and cell death. Cell Signal 18:592–600
Vivero-Salmeron G, Ballesta J, Martinez-Menarguez JA (2008) Heterotypic tubular connections at the endoplasmic reticulum-Golgi complex interface. Histochem Cell Biol 130:709–717
Voogd J, Glickstein M (1998) The anatomy of the cerebellum. Trends Neurosci 21:370–375
Vydra N, Winiarski B, Rak-Raszewska A, Piglowski W, Mazurek A, Scieglinska D, Widlak W (2009) The expression pattern of the 70-kDa heat shock protein Hspa2 in mouse tissues. Histochem Cell Biol 132:319–330
Waanders E, Croes HJ, Maass CN, te Morsche RH, van Geffen HJ, van Krieken JH, Fransen JA, Drenth JP (2008) Cysts of PRKCSH mutated polycystic liver disease patients lack hepatocystin but express Sec63p. Histochem Cell Biol 129:301–310
Wai MS, Shi C, Kwong WH, Zhang L, Lam WP, Yew DT (2008) Development of the human insular cortex: differentiation, proliferation, cell death, and appearance of 5HT-2A receptors. Histochem Cell Biol 130:1199–1204
Wakabayashi Y, Chua J, Larkin JM, Lippincott-Schwartz J, Arias IM (2007) Four-dimensional imaging of filter-grown polarized epithelial cells. Histochem Cell Biol 127:463–472
Walch A, Rauser S, Deininger SO, Hofler H (2008) MALDI imaging mass spectrometry for direct tissue analysis: a new frontier for molecular histology. Histochem Cell Biol 130:421–434
Walter B, Schlechter T, Hergt M, Berger I, Hofmann I (2008) Differential expression pattern of protein ARVCF in nephron segments of human and mouse kidney. Histochem Cell Biol 130:943–956
Wang L, Lee JF, Lin CY, Lee MJ (2008a) Rho GTPases mediated integrin alpha v beta 3 activation in sphingosine-1-phosphate stimulated chemotaxis of endothelial cells. Histochem Cell Biol 129:579–588
Wang P, Zhang H, Li W, Zhao Y, An W (2008b) Promoter-defined isolation and identification of hepatic progenitor cells from the human fetal liver. Histochem Cell Biol 130:375–385
Wang H, Wang S, Hu J, Kong Y, Chen S, Li L (2009) Oct4 is expressed in Nestin-positive cells as a marker for pancreatic endocrine progenitor. Histochem Cell Biol 131:553–563
Waschke J (2008) The desmosome and pemphigus. Histochem Cell Biol 130:21–54
Wiecek A, Adamczak M, Chudek J (2007) Adiponectin—an adipokine with unique metabolic properties. Nephrol Dial Transplant 22:981–988
Wiik A, Ekman M, Johansson O, Jansson E, Esbjornsson M (2009) Expression of both oestrogen receptor alpha and beta in human skeletal muscle tissue. Histochem Cell Biol 131:181–189
Wilhelm B, Brandenburger T, Post H, Aumuller G (2008) Expression and localization of PMCA4 in rat testis and epididymis. Histochem Cell Biol 129:331–343
Wilson PD, Goilav B (2007) Cystic disease of the kidney. Annu Rev Pathol 2:341–368
Wolburg H, Wolburg-Buchholz K, Sam H, Horvat S, Deli MA, Mack AF (2008) Epithelial and endothelial barriers in the olfactory region of the nasal cavity of the rat. Histochem Cell Biol 130:127–140
Wookey PJ, Zulli A, Hare DL (2009) The elevated expression of calcitonin receptor by cells recruited into the endothelial layer and neo-intima of atherosclerotic plaque. Histochem Cell Biol 132:181–189
Wustner D, Faergeman NJ (2008) Spatiotemporal analysis of endocytosis and membrane distribution of fluorescent sterols in living cells. Histochem Cell Biol 130:891–908
Xia Y, Lee K, Li N, Corbett D, Mendoza L, Frangogiannis NG (2009) Characterization of the inflammatory and fibrotic response in a mouse model of cardiac pressure overload. Histochem Cell Biol 131:471–481
Xu BZ, Lin SL, Li M, Zhu JQ, Li S, Ouyang YC, Chen DY, Sun QY (2009a) Changes in estrogen receptor-alpha variant (ER-alpha36) expression during mouse ovary development and oocyte meiotic maturation. Histochem Cell Biol 131:347–354
Xu XW, Pei SJ, Miao XR, Yu WF (2009b) Human signal peptide had advantage over mouse in secretory expression. Histochem Cell Biol 132:239–246
Yamada M, Kuwano K, Maeyama T, Hamada N, Yoshimi M, Nakanishi Y, Kasper M (2008) Dual-immunohistochemistry provides little evidence for epithelial-mesenchymal transition in pulmonary fibrosis. Histochem Cell Biol 129:453–462
Yamamoto N, Yang M, Jiang P, Tsuchiya H, Tomita K, Moossa AR, Hoffman RM (2003) Real-time GFP imaging of spontaneous HT-1080 fibrosarcoma lung metastases. Clin Exp Metastasis 20:181–185
Yokota S, Dariush Fahimi H (2009) Degradation of excess peroxisomes in mammalian liver cells by autophagy and other mechanisms. Histochem Cell Biol 131:455–458

Yu W, Centonze VE, Ahmad FJ, Baas PW (1993) Microtubule nucleation and release from the neuronal centrosome. J Cell Biol 122:349–359

Zei D, Pascarella A, Barrese C, Pantalone S, Stefanini S (2009) DEHP effects on retinal vessels in newborn rats: a qualitative and quantitative analysis. Histochem Cell Biol 132(5):567–575

Zhang B, Zhou Z, Lin H, Lv X, Fu J, Lin P, Zhu C, Wang H (2009) Protein phosphatase 1A (PPM1A) is involved in human cytotrophoblast cell invasion and migration. Histochem Cell Biol 132:169–179

Zhao Z, Tang L, Deng Z, Wen L, Jin Y (2008) Essential role of ADAM28 in regulating the proliferation and differentiation of human dental papilla mesenchymal cells (hDPMCs). Histochem Cell Biol 130:1015–1025

Zimmermann H (2006) Ectonucleotidases in the nervous system. Novartis Found Symp 276:113–128; discussion 128–130, 233–237, 275–281

Zimmermann DR, Dours-Zimmermann MT (2008) Extracellular matrix of the central nervous system: from neglect to challenge. Histochem Cell Biol 130:635–653