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EDITORIAL

In focus in HCB

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In this last Editorial in 2020, we highlight three manuscripts covering fields as diverse as the posttranscriptional regulation of the *Pou5f1/Oct4* gene during oogenesis and early embryogenesis, tubulin-binding cofactors and their modifications during mouse cochlear development, and a novel immunohistochemical detection protocol. Furthermore, we present the feature "Most popular articles published in HCB in 2018", which is based on the number of pdf downloads during the following two years. Springer Nature is a signatory to the San Francisco Declaration on Research assessment (DORA) and provides various article- and journal-level metrics for *Histochemistry and Cell Biology* with the aim of offering a solid source for article and journal performance and impact.

Finally, as this most unsettling year comes to a close, the Editors and the Editorial Board extend their wishes to all for a safe and healthy 2021.

Most popular articles published in HCB in 2018

The number of pdf downloads is one among other criteria to assess the overall impact of a scientific publication. As we began with the Editorial in December 2019 (Taatjes and Roth 2019) for the publications in HCB in 2017, here we look at the manuscripts published in 2018 in HCB to ascertain their appreciation by our readership during the following 2 years. Noteworthy, 29.35% of the published papers fell into the category ≥ 1000 times downloaded (Table 1), and 26.60% were downloaded between 500 and 999 times. Table 1 unambiguously demonstrates that the published articles cover the fields of traditional and modern histochemistry, advanced immunolabeling and in situ molecular techniques and their manifold applications in basic and applied bio-medical research. The four topmost downloaded papers are highly illustrative of this fact and include, "The peroxisome" by Islinger et al. (2018), "The micromechanics of lung alveoli" by Knudsen and Ochs (2018), "Clathrin-independent endocytosis" by Sandvig et al. (2018) and "Molecular imaging with nanoparticles" by Thurner and Debbage (2018). A Special Issue on "Hard Tissue Biology" edited by Amizuka and Kitazawa (2018) comprehensibly covered the molecular and cell biology of development, regeneration and metabolism of bone, cartilage and teeth (Goltzman 2018; Haraguchi et al. 2018; Hasegawa 2018; Ikeda et al. 2018; Komori 2018; Liu et al. 2018; Nakatomi et al. 2018; Nishimura et al. 2018; Ono and Nakashima 2018) and their pathology (Kitazawa et al. 2018a; Lui et al. 2018; Nishimura et al. 2018), aspects of tissue engineering (Hoshi et al. 2018), and, last but not least, the application of advanced intravital multiphoton imaging (Mizuno et al. 2018) and FIB-SEM (Hasegawa et al. 2018). Further noticeable and highly read papers reported on various aspects of COPII-dependent ER export (McCaughey and Stephens 2018), the intermediate compartment (Saraste and Marie 2018), contact-mediated cell communication by cytonemes and tunneling nanotubes (Mattes and Scholpp 2018), the mammalian centrosome (Schatten and Sun 2018), nuclear actin (Bajusz et al. 2018), the nucleolus (Schöfer and Weipoltshammer 2018; Stachecka et al. 2018; Stępiński 2018), open questions of nuclear organization and genome architecture (Adriaens et al. 2018), the epigenome (Kitazawa et al. 2018b; Uličná et al. 2018), human trophoblast invasion (Hiden et al. 2018; Moser et al. 2018), cell migration in the cerebellum (Schilling 2018), enteroendocrine cells (Fothergill and Furness 2018), monoamines of the enteric nervous system (Neuhuber and Wörl 2018), cannaboid receptors of the gastrointestinal tract (Galiazzo et al. 2018), protein glycosylation and glycophenotyping (Kaltner et al. 2018; Yamanoi and Nakayama 2018), autophagy (Eberhart and Kovacs 2018;

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Table 1 Most popular articles published in *Histochem Cell Biol* in 2018

*n**	Article
6878	Islinger et al.: The peroxisome: an update on mysteries 2.0. (Islinger et al. 2018)
6330	Knudsen and Ochs: The micromechanics of lung alveoli: structure and function of surfactant and tissue components. (Knudsen and Ochs 2018)
4916	Sandvig et al.: Clathrin-independent endocytosis: an increasing degree of complexity. (Sandvig et al. 2018)
4201	Thurner and Debbage: Molecular imaging with nanoparticles: the dwarf actors revisited 10 years later. (Thurner and Debbage 2018)
4137	Komori: Runx2, an inducer of osteoblast and chondrocyte differentiation. (Komori 2018)
3512	Schöfer and Weipoltshammer: Nucleolus and chromatin. (Schöfer and Weipoltshammer 2018)
3491	Gonçalves et al.: Development of a method for the detection of polystyrene microplastics in paraffin-embedded histological sections. (Gonçalves et al. 2018)
3365	Ono and Nakashima: Recent advances in osteoclast biology. (Ono and Nakashima 2018)
3347	McCaughey and Stephens: COPII-dependent ER export in animal cells: adaptation and control for diverse cargo. (McCaughey and Stephens 2018)
3266	Pirozzi et al.: ColorEM: analytical electron microscopy for element-guided identification and imaging of the building blocks of life. (Pirozzi et al. 2018)
3004	Moser et al.: Human trophoblast invasion: new and unexpected routes and functions. (Moser et al. 2018)
2676	Stachecka et al.: Nuclear organization during in vitro differentiation of porcine mesenchymal stem cells (MSCs) into adipocytes. (Stachecka et al. 2018)
2675	Stępiński: The nucleolus, an ally, and an enemy of cancer cells. (Stępiński 2018)
2362	de Beer et al.: A small protein probe for correlated microscopy of endogenous proteins. (de Beer et al. 2018)
2347	Luckner and Wanner: Precise and economic FIB/SEM for CLEM: with 2 nm voxels through mitosis. (Luckner and Wanner 2018)
2293	Zupkovitz G, Lagger S, Martin D et al. Histone deacetylase 1 expression is inversely correlated with age in the short-lived fish *Nothobranchius furzeri*. (Zupkovitz et al. 2018)
2197	Goltzman: Functions of vitamin D in bone. (Goltzman 2018)
2141	Saraste and Marie: Intermediate compartment (IC): from pre-Golgi vacuoles to a semi-autonomous membrane system. (Saraste and Marie 2018)
1881	Mattes and Scholpp: Emerging role of contact-mediated cell communication in tissue development and diseases. (Mattes and Scholpp 2018)
1593	Liu et al.: Inflammation, mesenchymal stem cells and bone regeneration. (Liu et al. 2018)
1484	Hiden et al.: Expression of matrix metalloproteinase 12 is highly specific for non-proliferating invasive trophoblasts in the first trimester and temporally regulated by oxygen-dependent mechanisms including HIF-1A. (Hiden et al. 2018)
1456	Adriaens et al.: Blank spots on the map: some current questions on nuclear organization and genome architecture. (Adriaens et al. 2018)
1442	Hasegawa: Ultrastructure and biological function of matrix vesicles in bone mineralization. (Hasegawa 2018)
1384	Jankowska-Steifer et al.: Cells with hematopoietic potential reside within mouse proepicardium. (Jankowska-Steifer et al. 2018)
1371	Erickson et al.: Soluble mucus component CLCA1 modulates expression of leukotactic cytokines and BPIFA1 in murine alveolar macrophages but not in bone marrow-derived macrophages. (Erickson et al. 2018)
1339	Groeneweg et al.: Gephyrin: a key regulatory protein of inhibitory synapses and beyond. (Groeneweg et al. 2018)
1194	Rezaei et al.: The expression of VE-cadherin in breast cancer cells modulates cell dynamics as a function of tumor differentiation and promotes tumor–endothelial cell interactions. (Rezaei et al. 2018)
1161	Nishimura et al.: Transcriptional network systems in cartilage development and disease. (Nishimura et al. 2018)
1056	Eberhart and Kovacs: Pexophagy in yeast and mammals: an update on mysteries. (Eberhart and Kovacs 2018)
1016	Galiazzo et al.: Localization of cannabinoid receptors CB1, CB2, GPR55, and PPARα in the canine gastrointestinal tract. (Galiazzo et al. 2018)
1010	Jühlen and Fahrenkrog: Moonlighting nuclear pore proteins: tissue-specific nucleoporin function in health and disease. (Jühlen and Fahrenkrog 2018)
1004	Schatten and Sun: Functions and dysfunctions of the mammalian centrosome in health, disorders, disease, and aging. (Schatten and Sun 2018)

*Threshold number of pdf downloads ≥ 1000 as per 7 November 2020

Offei et al. 2018), and dietary phosphate toxicity (Erem and Razaque 2018). The published manuscripts reporting methodical advancements covered a wide range of topics such as a method for the detection of polystyrene microplastics by Gonçalves et al. (2018), a technique for simultaneous identification of enzyme protein and activity by Villamonte

et al. (2018), an epitope-mediated in vivo MMP activation assay applied to zebrafish embryos by Jeffrey and Crawford (2018), holography microscopy by Pastorek et al. (2018), ColorEM for analytical electron microscopy by Pirozzi et al. (2018), a small protein probe for correlated microscopy by de Beer et al. (2018), precise and economic FIB/SEM for CLEM by Luckner and Wanner (2018), sensitive fluorescent hybridization protocol by Kovacs-Valasek et al. (2018), automated segmentation and quantitative shape analysis of confocal micrographs (Kopanja et al. 2018), computational simulation and modeling of the blood–brain barrier pathology (Shityakov and Förster 2018), as well as volume scanning electron microscopy for 3D reconstruction (Vanslembrouck et al. 2018).

The overall impact of the papers published in *Histochemistry and Cell Biology* is also reflected in the 2 year 2019 journal impact factor of 3.418. We would like to thank all of the authors for contributing their work leading to the success of *Histochemistry and Cell Biology*.

Posttranscriptional regulation of the *Pou5f1/Oct4* gene during oogenesis and early embryogenesis

Eukaryotic transcription factors containing a bipartite DNA binding domain referred to as the POU domain have important functions during development. Pou5f1/Oct4 is a member of the POU transcription factor family and is specifically expressed in germ cells and early embryonic cells in mouse (Scholer et al. 1989; Okamoto et al. 1990). In the present study, Takada et al. (2020) have established the time course of expression of maternal *Pou5f1/Oct4* mRNA and Pou5f1/Oct4 protein during oogenesis and early stages of embryogenesis in mouse ovaries and oviducts by using a highly sensitive in situ hybridization method and a monoclonal antibody specific to Pou5f1/Oct4 (Fig. 1).

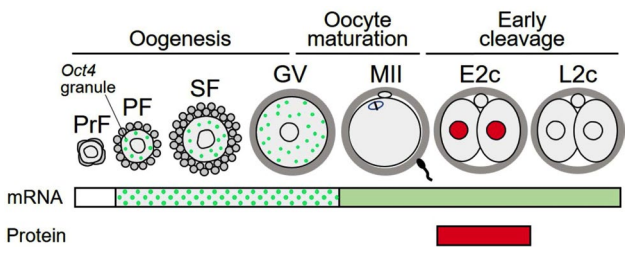

Fig. 1 Immunohistochemical Mdg1/ERdj4 protein pattern in the paraxial mesoderm. From Takada et al. (2020)

The authors found that *Pou5f1/Oct4* mRNA began to accumulate into RNA granules in oocytes at primary and secondary follicle stage and remained detectable up to the fully grown germinal vesicle stage. At all times, follicle cells showed no hybridization signal. The *Pou5f1/Oct4* RNA granules disappeared in MII-stage oocytes and in two-cell stage embryos. Since the mRNA amount did not change significantly, it was concluded that RNA granules disassembled rather than mRNA was degraded. By immunofluorescence and Western blotting, Pou5f1/Oct4 protein was not detectable during oogenesis, oocyte maturation and the first cleavage stage. It only became detectable in the nuclei of early two-cell stage embryos. Therefore, the authors proposed that the translation of cytoplasmic mRNA is repressed during oogenesis and up to the first cleavage stage. Taken together, this indicates the existence of posttranscriptional regulation of the *Pou5f1/Oct4* gene during oogenesis and early embryogenesis.

Tubulin-binding cofactors and their modifications during mouse cochlear development

Microtubules are a crucial component of the cell cytoplasm, playing a critical role in cellular functions as mitosis, vesicle transport, and maintaining cell shape. They are composed of alpha- and beta-heterodimers of tubulin and display various post-translational modifications. Tubulin synthesis itself is assisted by five tubulin-binding cofactors designated TBCA-TBCE, and the dysfunction of these proteins has been noted in various diseases, among them hearing loss. The organ of Corti housed within the cochlea is the center for hearing within the inner ear. During development, multiple precursor cells are found within the organ of Corti which will eventually differentiate into neurons, sensory hair cells, supporting cells and the otic epithelium (Fritzsch et al. 2015). Juergens and colleagues (2020) have performed very detailed immunofluorescence investigations on postnatal developing mouse cochlea aimed at (1) examining the cell- and temporal-specific expression patterns of TBC proteins, and (2) determining if there is a spatio-temporal change in the expression of tublin post-translational modifications. They chose to investigate mice at postnatal days 1, 7, and 14 (P1, P7, P14) due to specific developmental hallmarks in microtubule expression and onset of hearing. They validated the many antibodies used via Western blotting and immunohistochemical controls, and compared their results with those previously published on developing gerbil cochleae (Hallworth and Luduena 2000; Jensen-Smith et al. 2003; Tannenbaum and Slepecky 1997). The results of their multiple antibody combination staining on both paraffin sections and wholemount cochlear preparations visualized by confocal microsopy are beautifully illustrated with accompanying interpretive drawings (Fig. 2).

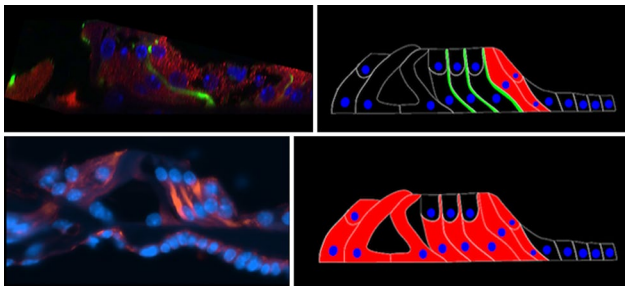

Fig. 2 Top row: distribution of tubulin-binding cofactors in P14 organ of Corti (red = TBCA; blue = DAPI; green = beta-tubulin). Bottom row: distribution of tubulin post-translationally modified proteins in P14 organ of Corti (red = tyrosinated tubulin; blue = DAPI). From Juergens et al. (2020)

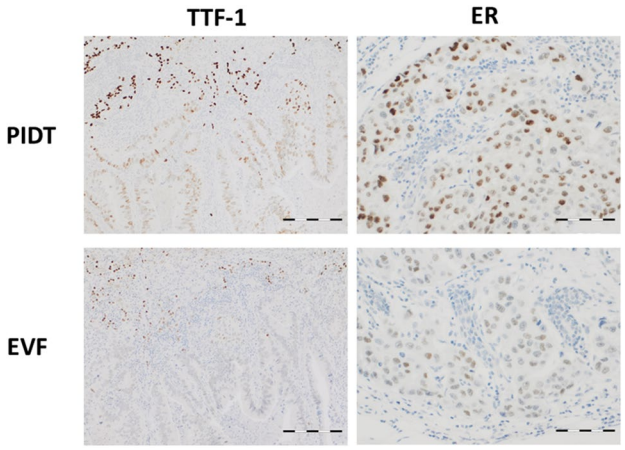

Fig. 3 Examples for PIDT and EnVision FLEX staining results of poorly fixed tissue (lung adenocarcinoma and breast cancer stained with TTF-1 or ER, respectively). From Seidl et al. (2020)

They found similarities, but also strong differences in the spatio-temporal expression of post-translationally modified tublulin forms between postnatal developing gerbil and mouse cochleae. Moreover, in this first ever investigation of tubulin binding cofactor proteins and tubulin post-translational modifications in the cochleae of developing mouse pups, the authors found a variety of staining patterns, in which no cell-type specificity could be deduced.

Novel immunohistochemical detection protocol

Immunohistochemistry has evolved as a key element in the pathologist's toolbox for disease diagnosis. Over the years, a wide variety of immunostain detection enhancement protocols, such as the tyramide-based system (Toda et al. 1999), have been developed with the goal of optimizing the visualization of staining results. Seidl and colleagues (2020) have now assessed a novel prototype immunohistochemical detection technology (PIDT) based upon a modification of an improved tyramide protocol (Lohse et al. 2014) for the visualization of antigenic sites in paraffin-embedded tissue sections. Essentially, this new PIDT protocol employs DAB as a cross-linker in a first deposition step resulting in a weak primary DAB stain which then anchors multiple FITC reporters available for a subsequent DAB stain with anti-FITC/HRP. For evaluating this new technology, the authors immunostained sections from a variety of tumor types with a large number ($n = 30$) of antibodies, some under differing fixation protocols (including sub-optimal). Results of the staining were assessed semi-quantitatively according to the following parameters: (1) signal distribution; (2) stain intensity; (3) tissue and background stain; (4) stain acutance (sharpness of stain image); (5) clarity of stain details; and (6) subcellular details of morphology, and compared to those obtained by a standard and widely used detection system (EnVision FLEX; Sabattini et al. 1998). Their experiments, with rigorous controls and protocol reproducibility included, showed that compared to conventional immunostaining protocols, PIDT processing resulted in (1) more rapid turnaround time due mostly to shorter incubation with the primary antibody; (2) enhanced stain signal intensity; (3) uniform signal distribution throughout the section; and (4) better staining results on suboptimally preserved tissue samples (Fig. 3).

Therefore, this new PIDT protocol, which will be made available by Agilent Technologies, should be a useful addition to diagnostic laboratories due to the improved processing turnaround time and tissue staining characteristics.

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News

Springer Nature and *Histochemistry and Cell Biology*

are proud to announce that the

Histochemistry and Cell Biology Lecture 2021

at the 16th International Congress of Histochemistry and Cytochemistry in Prague, Czech Republic will be delivered by

Professor Takehiko Koji
Nagasaki University Graduate School of Biomedical Sciences
Nagasaki, Japan

"Global changes in epigenomes and their significance in mouse spermatogenesis"

The Robert Feulgen Prize 2020 of the Society for Histochemistry

has been awarded ex aequo to

Dr. Christian Mühlfeld
Hannover Medical School, Hannover, Germany

for the development of new stereological and 3D image analysis techniques and their application to the quantitative analysis of the lung alveolar capillary network.

Dr. Hari Shroff
National Institute of Biomedical Imaging and Bioengineering, NIH, Bethesda, MD, USA

for significant improvement of spatial resolution and speed of image acqui- sition for super-resolution microscopes and their application in the generation of a 4D atlas of neurodevelopment in *C. elegans* embryos.

The Editors of *Histochemistry and Cell Biology* wish to convey their heartfelt congratulations to Drs. Mühlfeld and Shroff on the receipt of this honor.

https://www.microscopy-conference.de/

Invitation

Dear Colleagues,

It is a great pleasure to officially invite you to participate in the Microscopy Conference 2021 (MC2021), held in Vienna, Austria, from August 22 to 26, 2021. After the very successful preceding meetings MC2009 in Graz and MC2013 in Regensburg, MC2021 will be a combined conference of Dreiländertagung and Multinational Congress on Microscopy again. The conference will be jointly organised by ten microscopy societies from 11 countries (Austria, Croatia, Czech Republic, Germany, Hungary, Italy, Serbia, Slovakia, Slovenia, Switzerland and Turkey).

The MC2021 aims at bringing together leading experts and emerging young researchers, highlighting new developments in instrumentation and methods as well as providing a forum for new directions in the field of life or materials sciences. It will be an EMS extension, and it will focus especially on young scientists by providing very affordable fees. We are confident that at least 1,300 participants from all over Europe and overseas will attend the conference and guarantee a major scientific exchange.

The scientific programme will consist of plenary talks on important current topics. Latest developments in the fields of instrumentation and methods, materials science and life science will be highlighted by invited talks and also oral and poster presentations submitted. In addition to the scientific programme, workshops, an industrial exhibition, a conference dinner and award ceremonies in conjunction with award lectures will complement the programme.

The venue of MC2021 is the Congress Center Messe Wien, next to the Viennese Prater and within a 7-minute ride to the city center. The MC2021 will host a large exhibition, which aims to show the latest equipment from the manufacturers of all different kinds of microscopy and microscopy techniques, along with suppliers of consumables and accessories as well as publishers in the field. The exhibition will be embedded within the poster and catering area and will become an integral part of the conference.

Our goal is to organise a memorable microscopy event that gives you the opportunity of gathering information in science, networking and even perhaps enjoy some culture. We cordially welcome you to Vienna and to the MC2021!

Johannes Bernardi
Conference Chair

Michael Stöger-Pollach
Conference Co-Chair

Stefan Löffler
Conference Co-Chair

Dear Colleagues,

In the light of the COVID-19 pandemic, the ICHC 2020 organizers and IFSHC Executive Council decided to postpone the ICHC 2020 to **5 - 8 September 2021**. The ICHC 2021 will take place as originally planned in the Cubex Centre, Prague, Czech Republic. The safety of all participants is our top priority. We are sorry for any inconvenience the postponement might have caused you.

The ICHC is held every four years under the auspices of the International Federation of Societies for Histochemistry and Cytochemistry (IFSHC), which continually strives to provide grounds for communication and cooperation among scientists all over the world in the areas of cyto- and histochemistry, cell and tissue biology, microscopy, pathology and other relevant fields.

The city of Prague, also known as the heart of Europe, provides easy access for scientists from all over the world. The congress venue, Cubex Centre Prague which offers technologically and visually unique space, promises to leave everyone with an unforgettable experience. Of course, Prague prides itself with its beautiful historical architecture, technical monuments, celebrated cafés, great food, and beer. This will be underlined by the ICHC gala dinner in the famous Art Nouveau Municipal House, and a free beer party organized in the premises of the Staropramen brewery.

We hope that you will join us in Prague to discuss together your latest achievements and that the venue will provide great opportunities for specialists at all levels of their career, bringing lots of opportunities for strengthening international collaborations. Special attention will be therefore given to the presentations of students. We also expect a rich commercial exhibition where new and emerging technologies will be presented.

We are delighted to inform you that the following speakers will present a lecture at the congress:

Stefan Hell, a Nobel Prize laureate, Max Planck Institute for Biophysical Chemistry, Germany (keynote speaker)
Alev Erisir, Department of Psychology, University of Virginia, USA
Toyoshi Fujimoto, Juntendo University, Nagoya, Japan
Hans-Joachim Gabius, Institute of Physiological Chemistry, Ludwig Maximilians University of Munich, Germany
Bozena Kamińska, Nencki Institute of Experimental Biology PAS Warszawa, Poland
Takehiko Koji, Department of Histology and Cell Biology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
Ohad Medalia, Department of Biochemistry, University of Zurich, Switzerland

See you all in Prague, September 2021!

Hinke Multhaupt, President of the IFSHC
Klara Weipoltshammer, President of the Society for Histochemistry
Pavel Hozak, Chair of the Local Organizing Committee

Contacts
We will keep the current domain:
www.ichc2020.com

If you have any questions about registration, please contact: registration@ichc2020.com

If you have any questions about abstracts, please contact: abstracts@ichc2020.com

Other inquiries and comments about the conference, please contact: info@ichc2020.com

ANNOUNCEMENT

The Society for Histochemistry

Invites scientists to apply for the 2021 Robert Feulgen Prize. The prize is awarded for an outstanding achievement in the field of histochemistry.

The contributions may be either towards the development of new histochemical and cytochemical techniques or in the application of existing technology towards solving important problems in biology and/or medicine. Addressed are scientists working in microscopical sciences (in the widest sense) as well as in biochemistry, cell biology, endocrinology, in situ molecular techniques, and neurosciences. Scientists in their mid-career (assistant or associate professor, priv. doz.) are encouraged to apply. The prize is not intended for lifetime contributions.

The Prize consists of a monetary prize of €2,000

All applications should be submitted before January 31, 2021 via the electronic submission system at: https://www.greception.com/form-login-window/191a281d/

The application should contain a short curriculum vitae, a 1,000 word summary of the contributions of the applicant and PDF reprints of the pertinent publications. Full description of conditions is available on the Society website: http://histochemistry.eu/description_of_conditions_.html