Histochem Cell Biol (2017) 147:413–414
DOI 10.1007/s00418-017-1552-x

EDITORIAL

In focus in HCB

Douglas J. Taatjes[1] · **Jürgen Roth**[2]

Accepted: 15 February 2017 / Published online: 11 March 2017

The Golgi apparatus (GA) is a complex and highly dynamic organelle, which has been in focus in HCB previously (September 2013, Issue 3, pp. 233–367; October 2013, Issue 4, pp. 369–505). Following their earlier investigations (Meisslitzer-Ruppitsch et al. 2011; Ranftler et al. 2015) using the nonmetabolizable glucose analogue 2-deoxy-D-glucose (2DG) to analyze GA dynamics, Ranftler et al. (2017) applied high-resolution 3D-electron tomography to provide a detailed time course of 2DG-caused GA stack dispersal. Within 1 h of 2DG treatment, the GA cisternal stack was replaced by partly vesicular, tubular, and cisternal Golgi bodies. Following 2DG removal, these Golgi bodies provided the basis for the reformation of typical GA cisternal stacks through the intermediate stage of mini stacks. The highly detailed 3D analysis clearly showed connections linking tubular membranes during all phases of GA dispersal and reformation and their possible function in signaling or trafficking merits further studies.

Rab proteins and their interacting proteins are important regulators of membrane traffic. The YIP family (YIPF) of Rab-interacting proteins is ubiquitously expressed in human tissues. Kranjc et al. (2017) carried out a systematic localization analysis of the seven members of the YIPF protein family by studying GFP-tagged YIPF proteins. In transfected HeLa cells, through advanced quantitative co-localization analysis with the *cis*-Golgi marker GM130 and the TGN-marker TGN46, YIPF1 and YIPF2 were predominantly localized to the *cis*-Golgi apparatus, and YIPF3, YIPF4, and YIPF5 predominantly to the *trans*-Golgi, whereas YIPF6 and YIPF7 displayed a broad Golgi apparatus distribution. In addition, YIPF1 and YIPF2 localized with endosomal Rab GTPases indicative of their association with late endosomes and lysosomes. YIPF5 additionally co-localized with Rab1A involved in ER-to-Golgi apparatus trafficking. The depletion by RNA interference of *cis*-Golgi localized YIPF proteins induced Golgi apparatus fragmentation and fragment displacement. In contrast, depletion of *trans*-Golgi localized YIPF proteins did not induce Golgi apparatus fragmentation, but rather caused an increase in organelle area. Thus, the various YIPF proteins appear to be involved in the regulation of Golgi membrane dynamics. By a fluorescence protease protection assay, the N terminus of YIPF proteins was determined to be oriented in the cytosol and the C terminus to the Golgi cisternal lumen.

Vertebrate limb formation is widely viewed as a model system for investigating mechanisms of apoptosis. To date, most of these studies have focused on only the intrinsic (mitochondrial) apoptotic pathway, with little attention paid to the extrinsic (receptor-mediated) pathway. Since caspase proteins have been implicated in aspects of interdigital tissue elimination, Svandova et al. (2017) sought to investigate the role of the extrinsic receptor-mediated apoptotic pathway during mouse interdigital webbing regression. Using immunofluorescence and PCR array analyses, they examined the presence of Fas, Fas ligand, and caspase-8 in mouse forelimbs during the crucial time period between embryonic days 11 and 13. TUNEL staining was performed simultaneously as an indicator of cellular apoptosis. Very limited apoptosis was observed in samples from embryonic day 11, whereas intense areas of apoptosis were detected by embryonic day 13. Likewise, the amount of

✉ Douglas J. Taatjes
douglas.taatjes@uvm.edu

[1] Department of Pathology and Laboratory Medicine, The University of Vermont College of Medicine, Burlington, VT 05405, USA

[2] University of Zurich, 8091 Zurich, Switzerland

fluorescence staining for Fas, Fas ligand, and caspase-8 was found to increase across these embryonic days, with the most intense signal detectable at embryonic day 13 when interdigital tissue retraction has begun. These results were also mirrored by PCR analysis of multiple extrinsic apoptotic pathway markers, whereby expression of *Fas* and *caspase-8* amongst others was found to increase from embryonic day 11 through 13. Thus, these results suggest that the heretofore not widely investigated receptor-mediated extrinsic apoptotic pathway may be playing a critical role in vertebrate limb digitalization.

Much like vertebrate limb development, organ tissue development, including that of kidney is a highly complex and orchestrated process. Many types of human kidney disease involve glomerular alterations, often targeting podocytes in particular. Given the critical importance of this renal cell type in health and disease, and since much remains to be learned concerning podocyte differentiation and development in humans, Filipovic et al. (2017) have now performed a systematic characterization of podocytes during normal embryonic development, and in healthy postnatal and diseased nephrotic syndrome of the Finnish type. Since cytoskeletal proteins are known to be involved in podocyte differentiation processes of first mesenchymal-to-epithelial (MET) transition, and later epithelial-to-mesenchymal (EMT) transition, the authors used semi-quantitative multiple-staining immunofluorescence microscopy on paraffin sections to examine the expression of several of these proteins (nestin, cytokeratin 10, vimentin, and α-smooth muscle actin) during this differentiation process. Moreover, due to increased glomerular vascularization occurring during development, they also stained sections for the vascular markers CD31 and VEGF. Podocyte function itself was assessed by staining for receptor for advanced glycation end products (RAGE). During development, in differentiating podocytes the amount of nestin staining decreases, cytokeratin-10 decreases and eventually is no longer detectable, whereas vimentin staining was found to increase. As vasculogenesis ensues, the amount of α-smooth muscle actin and CD31 increased, while VEGF decreased. Further, as podocytes continued to differentiate, the RAGE immunostaining diminished. In tissues from diseased nephrotic syndrome of the Finnish type, immunostaining for α-smooth muscle actin and nestin was found to be enhanced, whereas that for CD31 was decreased. Transmission electron microscopy was also performed to provide ultrastructural details of podocyte features during differentiation. The data provided by this very detailed analysis of podocyte differentiation may aid in future attempts to treat damaged podocytes in a variety of kidney diseases.

References

Filipovic N, Vukojevic K, Bocina I, Saraga M, Glavina Durdov M, Kablar B, Saraga-Babic M (2017) Immunohistochemical and electronmicroscopic features of mesenchymal-to-epithelial transition in human developing, postnatal and nephrotic podocytes. Histochem Cell Biol. doi:10.1007/s00418-016-1507-7

Kranjc T, Dempsey E, Cagney G, Nakamura N, Shields DC, Simpson JC (2017) Functional characterization of the YIPF protein family in mammalian cells. Histochem Cell Biol. doi:10.1007/s00418-016-1527-3

Meisslitzer-Ruppitsch C, Röhrl C, Ranftler C, Neumüller J, Vetterlein M, Ellinger A, Pavelka M (2011) The ceramide-enriched trans-Golgi compartments reorganize together with other parts of the Golgi apparatus in response to ATP-depletion. Histochem Cell Biol 135:159–171. doi:10.1007/s00418-010-0773-z

Ranftler C, Meisslitzer-Ruppitsch C, Stangl H, Röhrl C, Fruhwürth S, Neumüller J, Pavelka M, Ellinger A (2015) 2-Deoxy-D-glucose treatment changes the Golgi apparatus architecture without blocking synthesis of complex lipids. Histochem Cell Biol 143:369–380. doi:10.1007/s00418-014-1297-8

Ranftler C, Meisslitzer-Ruppitsch C, Neumüller J, Ellinger A, Pavelka M (2017) Golgi apparatus dis- and reorganizations studied with the aid of 2-deoxy-D-glucose and visualized by 3D-electron tomography. Histochem Cell Biol. doi:10.1007/s00418-016-1515-7

Svandova EB, Vesela B, Lesot H, Poliard A, Matalova E (2017) Expression of Fas, FasL, caspase-8 and other factors of the extrinsic apoptotic pathway during the onset of interdigital tissue elimination. Histochem Cell Biol. doi:10.1007/s00418-016-1508-6