Histochem Cell Biol (2017) 148:1–2
DOI 10.1007/s00418-017-1586-0

EDITORIAL

In focus in HCB

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

Accepted: 30 May 2017 / Published online: 6 June 2017
© Springer-Verlag Berlin Heidelberg 2017

Mast cells are a type of white blood cell with a known role in pathologies such as allergic inflammatory conditions. They are normally identified microscopically in tissue sections stained with toluidine blue, where their cytoplasmic granules display a rich reddish-purplish hue. However, apparently not all mast cells from all animal species and all anatomic locations stain well with toluidine blue, leading to the introduction of histochemical and immunohistochemical methods to identify these cells more precisely. To help clarify this situation, Atiakshin and colleagues (2017) have evaluated a variety of staining techniques and methods to identify mast cells in various organs from human and rodent origin. They compared the number of mast cells identified in skin, stomach, small intestine, and liver in paraffin sections from humans, mice, and gerbils using (1) toluidine blue staining; (2) enzyme cytochemistry for chloroacetyl esterase; and (3) immunohistochemical detection of tryptase and chymase. Their results found that in general the immunohistochemical staining for tryptase and chymase provided the most objective assessment of mast cell populations in both human and rodent tissues. Metachromatic staining with toluidine blue also yielded good results. Variabilities in mast cell populations revealed by the different staining protocols were observed amongst tissue origins and species specificities. The staining obtained with the different methods clearly indicates the phenotypic state of the mast cell, partially reflecting the microenvironment presented by the tissue. Thus, it appears that the combination of metachromatic, immunohistochemical, and enzyme cytochemical staining approaches will prove useful for not only quantitating mast cell populations in various tissues and organs, but also for characterizing their phenotypic state.

The blood–brain barrier (BBB) is a highly selective filter that strongly limits the passage of molecules from the blood stream to the brain parenchyma, and this poses a problem for the application of neurotherapeutics. There are conflicting data whether receptor-mediated transcytosis can be exploited to transport macromolecules across the BBB. In continuation of their previous studies (Cabezón et al. 2015) applying 20 nm gold particles coated with the anti-transferrin receptor monoclonal antibody 8D3, Cabezón and colleagues (2017) have analyzed the uptake and distribution of 8D3-gold complexes in endothelia of brain capillaries using serial block-face scanning electron microscopy. Through optimized imaging protocols and 3D reconstructions, they now show that most of the gold particles become endocytosed, and after fusion of the endocytic vesicles are contained in large and complex structured endocytic vesicular networks. These results reinforce the concept that receptor-mediated transcytosis can be exploited for drug delivery across the BBB and show that serial block-face scanning electron microscopy is a useful tool for the 3D analysis of endocytic trafficking.

Müller cells in the retina are presumed to represent glia cells with progenitor-like characteristics. Since it is known that the transforming growth factor-β (TGF-β) pathway functions in maintaining adult neural stem and progenitor cells in a quiescent state (Kandasamy et al. 2011; Wachs et al. 2006), in continuation of their previous studies (Kugler et al. 2015), Kugler and colleagues (2017) analyzed whether an elevated TGF-β signaling has an

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

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

[2] University of Zurich, 8091 Zurich, Switzerland

influence on the proliferation of Müller cells in the developing retina. They generated mutant mice harboring a heterozygous deletion of *Smad7*, the inhibitor of TGF-β, which showed a systemic, heterozygous upregulation of TGF-β signaling. In the central part of the developing retina of the *Smad7*$^{\Delta/+}$ mutant mice, an increased proliferation of Müller cell progenitors was observed at postnatal day 4 that correlated with an increased SMAD3 phosphorylation. Furthermore, a significantly thickened retina and inner nuclear layer together with an increased number of differentiated Müller cells was obvious in the more developed retina. The Müller cells in juvenile mutant mice were strongly positive for nestin, indicating that they maintain some progenitor-like characteristics through the increased TGF-β signaling. Besides the increased Müller cell population, no other changes in the retinal phenotype could be observed. Hence, the authors conclude that TGF-β signaling not only promotes Müller cell proliferation during retina development, but additionally maintains them in a progenitor-like state in juvenile animals.

Cultured cell lines have been used for decades as in vitro models for specific cell types and tissues of origin. However, over time their characteristic phenotypic profiles may become altered, making them a less reliable model for their intended use. The cell lines Caco-2 and T84, both originally derived from a colonic tumor, have been used extensively as model epithelial cell barriers representing their colonic origins. However, evidence has suggested that Caco-2 cells are more reminiscent of small intestinal epithelial cells, while T84 cells have not been as extensively characterized. Devriese and colleagues (2017) have now performed experiments to more fully characterize these two cell lines by (1) comparing brush border morphology by transmission electron microscopy; (2) measuring the expression of enterocyte- and colonocyte-specific genes; and (3) assaying their response to butyrate challenge which requires the presence of the colonocyte epithelial membrane protein monocarboxylate transporter 1. Their results showed that (1) T84 cells displayed shorter microvilli than those observed in Caco-2 cells; (2) differentiated Caco-2 cells expressed mRNA profiles typical for small intestinal enterocytes (such as sucrose-isomaltase), while T84 cells expressed profiles associated with large intestinal colonocytes (such as membrane spanning 4-domains A12); and (3) T84 cells responded to butyrate in a dose-dependent manner as assessed by TEER measurements, whereas Caco-2 cells were not responsive. Together, their results demonstrate that differentiated Caco-2 cells possess characteristics associated with small intestinal epithelial cells, whereas T84 cells possess those of colonocytes. Their characteristic differences may have arisen due to the fact that Caco-2 cells were originally derived from a primary colonic tumor, while T84 cells were isolated from a lung metastasis. The authors therefore suggest that these differing morphological, biochemical, and transcriptional signatures be considered when selecting an intestinal epithelial cell model for specific experiments.

References

Atiakshin D, Samoilova V, Buchwalow I, Boeckker W, Tiemann M (2017) Characterization of mast cell populations using different methods for their identification. Histochem Cell Biol. doi:10.1007/s00418-017-1547-7

Cabezón I, Manich G, Martín-Venegas R, Camins A, Pelegrí C, Vilaplana J (2015) Trafficking of gold nanoparticles coated with the 8D3 anti-transferrin receptor antibody at the mouse blood-brain barrier. Mol Pharm 12:4137–4145

Cabezón I, Augé E, Bosch M, Beckett AJ, Prior IA, Pelegrí C, Vilaplana J (2017) Serial block-face scanning electron microscopy applied to study the trafficking of 8D3-coated gold nanoparticles at the blood–brain barrier. Histochem Cell Biol. doi:10.1007/s00418-017-1553-9

Devriese S, Van den Bossche L, Van Welden S, Holvoet T, Pinheiro I, Hindryckx P, De Vos M, Laukens D (2017) T84 monolayers are superior to Caco-2 as a model system of colonocytes. Histochem Cell Biol. doi:10.1007/s00418-017-1539-7

Kandasamy M, Reilmann R, Winkler J et al (2011) Transforming growth factor-beta signaling in the neural stem cell niche: a therapeutic target for Huntington's disease. Neurol Res Int 2011:124256. doi:10.1155/2011/124256

Kugler M, Schlecht A, Fuchshofer R et al (2015) Heterozygous modulation of TGF-β signaling does not influence Müller glia cell reactivity or proliferation following NMDA-induced damage. Histochem Cell Biol 144:443–455. doi:10.1007/s00418-015-1354-y

Kugler M, Schlecht A, Fuchshofer R et al (2017) SMAD7 deficiency stimulates Müller progenitor cell proliferation during the development of the mammalian retina. Histochem Cell Biol. doi:10.1007/s00418-017-1549-5

Wachs F-P, Winner B, Couillard-Despres S et al (2006) Transforming growth factor-beta1 is a negative modulator of adult neurogenesis. J Neuropathol Exp Neurol 65:358–370. doi:10.1097/01.jnen.0000218444.53405.f0