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EDITORIAL

In focus in HCB

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

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New details for predicting saphenous vein graft occlusion following CABG surgery

Coronary artery bypass grafting (CABG) is currently the method of choice for improving blood flow in the atherosclerotic vessel through surgical procedures. In younger patients (less than 65 years of age) a segment from the internal thoracic artery is classically used as the donor vessel for the graft, whereas in patients older than 65 years of age a section from the saphenous vein is typically chosen since it is less likely to undergo arterialization (Al-Sabti et al. 2013). Although much information is known concerning factors responsible for patency rates for internal thoracic artery donor vessels, very little is currently known about those responsible for saphenous vein patency in CABG procedures. However, since stem cell and progenitor cell proliferation in the graft wall have been shown to be involved in early saphenous vein graft occlusion (Timmermans et al. 2009), Malinska et al. (2017) performed a multivariate analysis of stem cell and progenitor cell markers in the donor saphenous vein wall prior to CABG procedure, followed by correlation with graft occlusion. Their results showed that strong immunohistochemical expression of CD133 (a stem cell marker) in smooth muscle cells of the tunica media of the graft correlated with early graft occlusion (within 12 months of the surgical procedure). Therefore, the authors suggest that screening of donor saphenous vein segments for CD133 immunohistochemical expression prior to CABG procedure might serve as a predictive indicator of potential early graft failure.

Thymocyte-thymic epithelial cell interactions in EphB-deficient mice

Epithelial free areas (EFA) are known to occur in both the cortex and medulla of the thymus in a variety of animal species. Whether the cortical and thymic EFAs represent the same or different histological and functional situations remains open for debate. Garcia-Ceca et al. (2017) have now investigated whether EFAs might represent microenvironments where thymocyte-thymic epithelial cell (TEC) interactions are disrupted, potentially resulting in altered thymic histology. As a model system, they employed EphB-deficient mice (EphB, a family of protein tyrosine kinases, and ephrins-B, their ligands are regulators of epithelial organization) previously shown by these authors to display altered thymocyte-TEC interactions (Garcia-Ceca et al. 2015). They used multilabel fluorescence microscopy, semiquantitative analysis, and transmission electron microscopy to evaluate the number and sizes of EFAs, as well as their organization and cell content in EphB-deficient mice compared to wild-type (WT) control animals. Their morphological results showed that: (1) in both WT and EphB-deficient mice, the number and size of EFAs were larger in the medulla compared to the cortex; (2) low numbers of EFAs correlate with larger areas; (3) EFA structure and cell content are similar in WT and EphB-deficient thymuses; and (4) EFAs in cortex and medulla contain different cell types and are structurally distinct with cortical areas possessing DP thymocytes and medullary regions SP thymocytes. Overall, their results suggest that EFAs in their model may be partially due to

✉ 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

epithelial cell degeneration resulting from the lack of EphB signaling altering cell–cell interactions therein. Moreover, the authors speculate that EFAs have no functional immunological significance, but rather indicate a dysregulation of thymic cell components leading to improper TEC maturation.

OATP1B3 and OATP2B1 transporter expression in human pancreatic islets

Organic anion-transporting polypeptides (OATPs) consist of 6 families and 13 subfamilies (Hagenbuch and Stieger 2013) and mediate the cellular uptake of many diverse endogenous and exogenous substrates. Although the expressions of the OATP1B1 and OATP1B3 transporters are assumed to be liver-specific, recent evidence (Meyer zu Schwabedissen et al. 2014) indicated the presence of the OATP1B3 transporter in pancreatic β cells. A detailed gene expression and immunohistochemical study by Kim et al. (2017) now shows high expression of OATP1B3, OATP2B1 and OATP1Al mRNA in human pancreatic islets, and a high association of OATP1B3 immunostaining with glucagon-producing pancreatic α cells. Less frequently, an association with insulin-producing β cells was detected. In contrast, immunostaining for OATP2B1 transporter was more often associated with insulin-producing β cells than with α cells. In addition, a two- to threefold higher percentage of OATP1B3 immunostaining of endocrine cells was observed in the islets of individuals of ≥60 years of age as compared to individuals of <60 years of age. Prominent OATP1B3 immunostaining was also detected in islets of patients with chronic pancretitis and pancreatic ductal adenocarcinoma, extending previous reports (Hays et al. 2013; Thakkar et al. 2013). The current findings provide a starting point to establish the function of OATPs in islets of Langerhans.

Immunohistochemical markers for quiescent human pancreatic stellate cells

Activated pancreatic stellate cells play an important role in the initiation of fibrosis in chronic pancreatitis and pancreatic cancer (Klöppel et al. 2004). Like hepatic stellate cells, they reside in a quiescent state in the normal pancreas and contain vitamin A lipid droplets (Apte et al. 1998; Bachem et al. 1998). In contrast to quiescent hepatic stellate cells, immunohistochemical markers for quiescent pancreatic stellate cells in formaldehyde-fixed and paraffin-embedded human tissue are lacking. Using human tissue microarrays and an extensive panel of antibodies, Nielsen et al. (2017) report now that cytoglobin and adipophilin are not only markers for quiescent hepatic but also for pancreatic stellate cells. Cytoglobin in human pancreas was expressed in two types of profibrogenic cells: quiescent stellate cells and resident interlobular fibroblasts. Of note, for reproducible strong adipophilin immunostaining, the pancreatic tissue had to be fixed in formaldehyde within 1 h after removal.

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