Virchows Archiv (2023) 482:461–462
https://doi.org/10.1007/s00428-023-03528-3

NEWS

In this issue

Published online: 14 March 2023

We would like to draw your attention to some articles in this issue which may be interesting for you.

Xu et al. (https://doi.org/10.1007/s00428-022-03422-4) studied poorly differentiated thyroid carcinomas (PDTC) from 2 different institutions for the impact of oncocytic features on various clinicopathological parameters and outcome (as illustrated on the cover page). Almost 40% of the tumors had an oncocytic cell component and about one quarter fulfilled the WHO cutoff of 75% for an oncocytic definition. Any oncocytic component and a 25% cut-off of oncocytic tumors cells were associated with decreased disease-specific and locoregional recurrence-free survival compared to non-oncocytic PDTC, both on univariate and multivariate analysis. Interestingly, a 100% cut-off showed statistical significance for disease-specific survival only on univariate analysis. A novel aspect in this study was that any oncocytic cut-off was associated with higher radioactive iodine -refractoriness compared to non-oncocytic PDTCs. PDTC with oncocytic features were also characterized by different molecular alterations compared to non-oncocytic PDTC, which showed statistical significance (*NF1* and *PTEN* alterations in oncocytic PDTCs versus *NRAS* mutations in non-oncocytic PDTC). This study endorses the distinct biology of oncocytic differentiation in thyroid tumors which is reflected by molecular features, radioactive iodine sensitivity and outcome. It has the potential to contribute to a further specification and clinically relevant subcategorization of poorly differentiated thyroid tumors of follicle cell differentiation.

Ohya et al. (https://doi.org/10.1007/s00428-023-03521-w) studied the cellular mechanisms involved in the development of diffuse alveolar damage (DAD) with special emphasis on CD8+ bystander T-lymphocytes. Non-antigen-activated bystander CD8 + T cells express the unique granzyme B (GrB) + /CD25-/programmed cell death-1 (PD-1)-phenotype. To study their involvement in the development of DAD, the authors analyzed autopsy specimens from patients with diffuse alveolar damage caused by sepsis, hemorrhagic and cardiogenic shock and hepatic failure for the phenotypes of infiltrating lymphocytes using immunohistochemistry. COVID-19 associated DAD was not included. In most cases, the number of CD8+ T cells was higher than that of CD4+ T cells, and many GrB + cells were also observed with differences in the various phases of DAD; but the number of CD25 + and PD-1 + cells was low. The authors conclude that bystander CD8+ T cells may contribute to the development of DAD; however, it remains unclear, whether they are the cause or effect of DAD. The cellular immune response based on the innate immune system involving bystander CD8 + T cells may play an important role in the formation of lesions in DAD. One interesting practical aspect coming up from this study is whether the cellular milieu in DAD might be a potential target for more effective therapeutic intervention in severe DAD. This will require further investigations both on experimental and clinical fields.

Yang et al. (https://doi.org/10.1007/s00428-023-03502-z) studied the role of deep learning based artificial intelligence in the histopathological diagnosis of prostate carcinoma with special emphasis on tumor recognition and tumor grading. The authors address that the problem of difficult cases with small tumor areas which can easily be missed on whole slide images. A major issue seems to be the method used for slide analysis. Existing methods usually perform uniform cropping of the foreground of whole slide images and then use convolutional neural networks as the backbone network to predict the classification results. However, cropping can damage the structure of tiny tumors and thereby affect classification accuracy. To solve this problem, the authors propose a novel supervised framework, designated as intensive sampling multi-instance learning (ISMIL), which focuses on tumor regions and improves the recognition of small tumor regions by intensively sampling the crucial regions. Testing of this method achieved a significant improve of the detection of difficult areas combined with higher specificity. The authors are optimistic that due to its robustness in independent cohorts, the method may become a potential tool to improve the diagnostic efficiency of pathology. However, the model has limitations including weaknesses in fine-grained visual interpretation of cancer subclasses and poor performance on Gleason grading. Future studies also

by independent groups will be needed to further develop and validate this model.

Agaimy et al. (https://doi.org/10.1007/s00428-022-03484-4) studied ACTH secreting neuroendocrine neoplasms of the pancreas and found that they are enriched for various gene fusions in contrast to their non pancreatic counterparts. The study included 21 neuroendocrine neoplasms mainly from the pancreas and the lung and used targeted RNA sequencing. The fusions involved *EWSR1::BEND2, KMT2A::BCOR* and *TFG::ADGRG7* and were mutually exclusive with *ATRX, DAXX*, and *MEN1* mutations. The findings unraveled by this study are quite interesting, particularly the gene fusions may play a role in triggering the ACTH production in pancreatic neuroendocrine neoplasms presenting with ectopic Cushing syndrome. The authors postulate that overexpressed fusion proteins might (e.g., via molecular homology with promotor genes) be involved in promoter-mediated overexpression of pre-ACTH precursors in analogy to mechanisms postulated for paraneoplastic phenomena in certain mesenchymal neoplasms. However, the genetic background of the ACTH-producing non-pancreatic NENs remains to be further studied.