# In this issue

This month's issue opens with a review by Chabot-Richards et al. (https://doi.org/10.1007/s00428-018-2501-3) on the use of molecular methods for Human Leukocyte Antigen (HLA) typing. Primary use of HLA typing is for solid organ and hematopoietic stem cell transplantation but lately the association of HLA types with specific diseases and its role in pharmacogenetics have gained in importance. Even though diagnostic use in histo- and cytopathology is virtually non-existent, the molecular methods are quite similar to those used for molecular genetic testing in a diagnostic pathology setting and might very well be performed in the same core facility.

Langer et al. (https://doi.org/10.1007/s00428-018-2482-2) elaborate an original take on the future of autopsies. They reason that beyond the well-known medical, legal and socio-economic factors responsible for ever-more declining autopsy rates, organization of space and workflow issues might be contributing factors. They redesigned their classical autopsy suite into a post-mortal diagnostic unit applying LEAN management principles. Rather than using classical autopsy techniques, operative diagnostic procedures were introduced, using laparotomy/scopy as well as thoracotomy/scopy approaches with minimally invasive intent. In addition, the workflow was revised to attain a significant reduction in turn-over time. These innovations led to a modest increase in the number of requested autopsies. The authors reason that changing from the 'classical autopsy' to 'post-mortal diagnostics' may improve the perception of post-mortal examinations by clinicians, relatives of a deceased as well the public at large and thus further development of the 'final consultation' for quality control of medical practice and for pre- and postgraduate education.

How immune-checkpoint function interferes with immunotherapy efficacy is intensely scrutinized in a variety of tumors and in this context Mandarano et al. (https://doi.org/10.1007/s00428-018-2483-1) studied the expression of indoleamine 2,3-dioxygenase 1 (IDO-1) and the programmed cell death ligand-1 (PD-L1) in non-small cell lung cancer. They correlated results of IDO-1 and PD-L1 immunostaining with the presence of tumor infiltrating lymphocytes, tumor histological type and outcome in terms of survival. They found associations between expression of IDO-1 and PD-L1 and histological type (more in poorly differentiated adenocarcinomas and in squamous cell carcinomas), smoking history, disease stage and density of tumor infiltrating lymphocytes, the presence of the latter also correlating with better prognosis. These findings contribute to explaining why poorly differentiated adenocarcinomas and squamous cell carcinomas have the capacity to escape an anti-tumor immune response.

Two papers in this issue address aspects of breast cancer pathology and both touch upon issues that go beyond breast cancer only. Del Rosario et al. (https://doi.org/10.1007/s00428-018-2481-3) revisit the Ki-67 proliferative index as a predictive and prognostic factor in breast cancer. This parameter is not universally accepted for daily practice because of reproducibility issues regarding its assessment, which has also hampered the procurement of sufficient evidence of clinical utility. The issue at stake is not limited to the Ki67 index in breast cancer; (semi)quantification of immunohistochemical staining results remains a serious problem in research studies but also in daily diagnostic practice. The authors tackled the problem by comparing scores of two pathologists, who each produced scores by global visual assessment ('eyeballing'), by digital image analysis in highly proliferative (hot spot) areas or as an average between proliferation high and proliferation low areas. It is not surprising that inter-pathologist concordance was better with digital image analysis in comparison with global visual assessment, notably in lesions with heterogeneous distribution of proliferative activity. Interestingly, averaging areas of low and of high proliferative activity did better than assessment of hotspots only. The authors advocate the use of the average approach by digital image analysis, notably in case of lesion with heterogeneous proliferative activity.

The cover image is from this paper and illustrates selection of Ki67 expressing cells in a breast cancer.

And then Jang et al. (https://doi.org/10.1007/s00428-018-2495-x) investigated how well the revised prognostic staging system for breast cancer, proposed in the 8th edition of the American Joint Committee on Cancer (AJCC 8), predicts outcome in comparison with the purely anatomy based

TNM stage. The AJCC approach incorporates tumor grade, as well as standard immunohistochemically assessed tumor characteristics (ER, PR, HER2) and also multigene assay results. This is a reflection of ongoing discussions between AJCC and UICC (as organization responsible for TNM) regarding staging, with as key question whether or not new staging approaches should amalgamate anatomic and molecular parameters. The conclusion of the study is that prognostic staging according to AJCC 8 more accurately predicts clinical outcome than conventional TNM staging.

The question remains whether this should be called prognostic stage. It may be wiser to keep the term stage for the purely anatomical (TNM) approach, which then in a second step can be completed with an additional layer of molecular parameters to define more detailed prognostic (sub)groups.