

In this issue

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This is the first issue of a new year for the journal and its readers, and the editorial team wishes its readers as much pleasure taking in the journal's content as it has in preparing the content. The issue opens with a very timely topic: tumor microenvironment and its impact on tumor behavior. Heiskala et al. (<https://doi.org/10.1007/s00428-018-2461-7>) studied this in breast cancer, focusing on tumor associated M2 macrophages, which favor tumor cell survival and proliferation and are pro-metastatic. Immunohistochemistry was applied to identify tumor associated macrophages as well as stromal and tumor cells expressing CCL2, the chemokine instrumental in recruitment and maturation of macrophages, in three patient cohorts with early, intermediate and late relapse. Tumor associated macrophages were found more around than in the tumors and more abundantly in recurrent than in primary lesions. This was accompanied by a higher number of cells expressing CCL2. Major finding was the association between early relapse and abundance of CCL2 expressing cells along with a high density of tumor associated macrophages. The authors suggest that early relapse might be countered by an anti-CCL2 approach, a notion which merits to be further explored.

In the study reported by Masashi et al. (<https://doi.org/10.1007/s00428-018-2476-0>) the starting point was the finding in silico that expression of ecotropic virus integration site 1 protein homolog (EVI1), known as oncogenic transcription factor for hematopoietic cells and contributor to cancer of the pancreas in inducing expression of KRAS, is also high in cholangiocarcinoma. By immunohistochemistry, the authors found expression of EVI1 in roughly half of intrahepatic cholangiocarcinomas and in all bile duct intraductal papillary neoplasms, regardless of histological grade or type. Moreover, indicators of aggressive behavior were more frequently found in intrahepatic cholangiocarcinomas expressing EVI1 than in those negative for this transcription factor. The authors conclude that expression of EVI1 is associated with aggressive behavior of intrahepatic cholangiocarcinomas, might be crucial in its molecular pathogenesis, and should be considered as target for therapy.

That certainly would require much more mechanism oriented investigation.

For some conditions classical morphological characteristics still need to be further detailed, as is illustrated in the study reported by De Vito et al. (<https://doi.org/10.1007/s00428-018-2464-4>), who provide further detail in the histological changes in the liver of patients with a congenital portosystemic shunt. They studied liver histology of a fairly large patient cohort from a single institution of this rare condition. Most characteristic were portal tracts with prominent thin walled channels, portal tracts with only an artery and a biliary duct and increased arterial profiles in portal tracts and lobule.

The cover image is from this paper and shows a portal tract with an interlobular bile duct and an arterial branch but absence of a portal vein.

Quality assurance in molecular testing is addressed in the paper of Hartmann et al. (<https://doi.org/10.1007/s00428-018-2480-4>). BRAF mutations figure prominently in a variety of tumors and their presence can be very relevant when it comes to selection of optimal treatment. The authors assessed impact of melanoma sample characteristics on the results of a BRAF mutation test, in a daily practice setting across most of the German diagnostic pathology centers performing molecular analyses. The idea was to test whether sample and/or patient characteristics would allow prediction of an expected BRAF mutation frequency. In their cohort, the authors were able to develop a statistical model allowing prediction of the frequency of BRAF mutations, which might subsequently be used as a benchmark. The idea is interesting and the chosen approach promising. Applicability of the reported approach, however, hinges on validation of the findings in an independent validation cohort.

Finally, Puripat and Loharamtaweethong (<https://doi.org/10.1007/s00428-018-2458-2>) studied the classical parameter of mitotic count in the context of establishing meningioma grade. A key problem in mitosis counting is a lingering lack of reproducibility in morphological recognition of mitotic figures, for which for example apoptotic figures might be taken. Phosphohistone H3 is expressed uniquely during mitosis and therefore antibodies specifically recognizing

phosphorylated histone H3 have been proposed as a tool for specific mitotic figure immunostaining. In this study the authors compared anti-phosphohistone antibodies recognizing different phospho-serines in comparison with morphological mitosis counting. A comforting result was the high correlation between morphological counting and counting based upon immunohistochemical staining. All used antibodies

performed well but with differences in absolute proportions of mitoses identified, which calls for antibody-specific cut-off values in terms of recurrence prediction.

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