## In this issue

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The complex mechanisms behind the biology of hematologic neoplasms have been earlier unraveled compared to solid tumors. Molecular studies have enormously broadened our understanding of these diseases and opened doors for efficient and targeted therapies. A review by Schürch et al. on multiple myeloma (https://doi.org/10.1007/s00428-019-02725-3) focusses in particular on the spatial heterogeneity of this neoplasm and the role of clonal evolution during disease progression. The former poses a challenge for classification and risk stratification and the latter may complicate disease monitoring and promote drug resistance. The identification and molecular characterization of the dominant diseasedriving neoplastic clones represents a key to optimal personalized therapy. Finally, the microenvironment of the bone marrow and the host immunity play an important role in the pathogenesis of multiple myeloma (illustrated on the cover page) in which multiple secretory proteins such as angiogenic factors and cytokines and cellular receptors are involved by a complex interaction.

Whereas the etiology of many neoplastic diseases including multiple myeloma is uncertain or at least not fully proven a subset of malignancies develops through viral tumorigenesis. As discussed by Fukayama et al. (https://doi.org/10.1007/s00428-019-02724-4) EBV non-coding RNAs and exosomes derived from EBV-infected cells have been recognized for their roles in the pathogenesis of EBV-associated gastric carcinoma, which accounts of about 10% of gastric carcinoma worldwide with geographic variability. On the cellular level the EBV, which is able to cause several mostly neoplastic diseases skillfully utilizes the cellular machinery to control the infected cells and their microenvironment. There is evidence that EBV associated gastric carcinoma, which is frequently deficient for the mismatch repair system and represents one of the 4 molecularly characterized gastric carcinoma

types in the TCGA can be successfully treated by immune checkpoint inhibitors.

A large multi-institutional study by scientists from Europe and Japan under guidance of Holger Moch (https://doi.org/10. 1007/s00428-019-02710-w) developed a novel two-tiered grading system for chromophobe renal cell carcinoma, in particular to detect the small subset of tumors with adverse prognosis. Using the presence of a sarcomatous (sarcomatoid) differentiation and tumor cell necrosis as components, the grading system turned out being both significant for overall survival and reproducible among multiple observers and within different cohorts, respectively.

The subgross morphology of breast carcinomas representing the distributions of the in situ and invasive components of the tumors as determined on large format histological sections assisted by radiological-pathological correlation may play an underestimated role even in the era of molecular-based tumor classification. Tibor Tot and colleagues from the Swedish Falun (https://doi.org/10.1007/s00428-019-02641-6) have been able to demonstrate on a large collective of cases that a complex morphology as present in multifocally and diffusely growing tumors is not only associated with adverse prognosis but may also correlate with the molecular type and finally influence therapeutic strategies.

Last but not least, two articles are dealing with practical aspects of the assessment of HER2 in carcinomas of the breast and the colon, respectively. Murray et al. (https://doi.org/10. 1007/s00428-019-02636-3) analyzed the impact of the 2018 ASCO/CAP recommendation on HER2 testing of breast carcinomas by FISH whereas Wang et al. (https://doi.org/10. 1007/s00428-019-02668-9) assessed two different scoring systems on colorectal carcinoma including their clinical relevance.

