In this issue

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This issue opens with a review on a subject that in daily life not many diagnostic pathologists will be concerned about but that has emerged as an essential element in our understanding of the biology of cancer: the role of the host stromal reaction. De Wever et al. (DOI [10.1007/s00428-015-1818-4](https://doi.org/10.1007/s00428-015-1818-4)) review the role of cancer-associated fibroblasts (CAF) as drivers of tumor progression and potential target and tool in diagnosis and treatment of cancer. A stromal response characterized by abundant CAFs is a hallmark of poor prognosis in several types of cancer. CAFs appear to play an important role in the tumor environment in terms of communication with cancer cells and other cells in the host response. New drugs targeting CAFs are in the pipeline. CAFs might even be used to capture circulating tumor cells before they metastasize.

Quieros et al. (DOI [10.1007/s00428-015-1823-7](https://doi.org/10.1007/s00428-015-1823-7)) took a close look at *KRAS* mutations in gastric cancer, against the background of anti-EGFR treatment, effective in *KRAS*wt colorectal cancer patients but not in gastric cancer patients. As in the latter, *KRAS* mutation status is not assessed as a rule; they sequenced the entire *KRAS* coding sequence in a series of microsatellite instable gastric cancers. About 1 in 4 gastric cancers carried a *KRAS* mutation invariably in the usual codons 12 and 13. The majority of *KRAS*-mutated cancers were heterogeneous in that *KRAS*wt as well as *KRAS*-mutated clones were found. The impact of this tumor heterogeneity on response to anti-EGFR treatment and the emergence of resistance need to be further clarified.

Keefe et al. (DOI [10.1007/s00428-015-1809-5](https://doi.org/10.1007/s00428-015-1809-5)) looked at prostate cancer patients with a Gleason Score 3+4=7 on a biopsy, which are considered candidate for active surveillance. An important question is whether histological features might be identified which predict extension of disease beyond the prostate in an eventual subsequent radical prostatectomy. Such features might then be a reason to upgrade the Gleason score and proceed to active intervention. While the features that predict upstaging of biopsy proven Gleason Score 3+4=7 prostate cancer remain somewhat elusive, the authors found the presence of cribriform pattern on prostate biopsy to be significantly associated with non-organ confined disease. This may provide a novel risk factor for improved risk stratification when making decisions regarding eligibility for active surveillance. The cover image is taken from this paper and represents such cribriform pattern in a prostate biopsy.

The paper by Krpina et al. (DOI [10.1007/s00428-015-1808-6](https://doi.org/10.1007/s00428-015-1808-6)) is somewhat related to the host response review paper that opens this issue. Their idea was to see if in solitary low-grade non-muscle invasive bladder cancer, the density of tumor-infiltrating leukocytes (TIL) is predictive for recurrence. It turns out that TIL occur predominantly in cancer stroma. CD3+ and CD8+ TIL were more numerous in the recurrent group of patients than in those that did not recur. This contrasts with what has been found in other cancers, in which a high number of TIL was associated with less aggressive disease. The authors suggest that CD3+ and CD8+ TIL are predictive of recurrence in patients with solitary low-grade non-muscle invasive bladder cancer. This needs confirmation in prospective studies before it might be included in the standard work-up of bladder cancer biopsies.

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