In this issue

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Is there anything that binds together the papers in anyone issue? Not really. The order of the published papers might be determined by an intention to regroup them according to theme. Otherwise, it is on a “first come, first served” basis. The first paper in the spotlight for this issue is the study of Ueno et al. ([10.1007/s00428-015-1756-1](https://doi.org/10.1007/s00428-015-1756-1)) on the response of rectal cancer to neoadjuvant radiochemotherapy. They focused on the desmoplastic reaction in the primary tumor, which they classified according to the characteristics of the extracellular matrix. In addition, CD8+ and FoxP3+ cells were identified by immunostaining to characterize the accompanying immune response. A matrix with multilayered collagen, which they called mature, was accompanied by more CD8+ and FoxP3+ cells. This pattern was also significantly and independently associated with a better pathological response and a longer 5-year disease-free survival. The paper thus emphasizes the increasing importance of the stromal response interrelated with the immune reaction to cancer as a determining factor in tumor behavior. The cover image is from this paper and illustrates the different patterns of desmoplastic reaction observed.

Hosoda and colleagues ([DOI 10.1007/s00428-015-1751-6](https://doi.org/10.1007/s00428-015-1751-6)) looked at GNAS mutations in intraductal papillary mucinous neoplasm (IPMN), in comparison with pancreatic carcinomas and pancreatic intraepithelial neoplasia (PanIN). In two thirds of IPMN and one third of IPMN-associated adenocarcinomas, a GNAS mutation was found. Furthermore, GNAS mutations were found in most mucinous carcinomas, with or without associated IPMN, but rarely in pancreatic ductal adenocarcinomas or PanIN and not at all in mucinous cystic neoplasms. The finding that IPMN and mucinous

carcinomas with or without associated IPMN frequently harbor a GNAS mutation provides solid evidence that these constitute a continuous spectrum of pancreatic tumors.

The spectrum of tumors responsive to HER2-targeting therapies is expanding, and Tschui et al. ([DOI 10.1007/s00428-015-1729-4](https://doi.org/10.1007/s00428-015-1729-4)) address histomorphology and molecular characteristics of HER2-expressing urothelial bladder cancer. In about 10 % of metastatic primary bladder cancers, HER2 amplifications were found; most of these tumors strongly expressed HER2 protein. One tumor harbored a mutation in the HER2 gene while all others were wild type.

Histomorphologically, HER2-amplified tumors were heterogeneous and yet much more often micropapillary than HER2-non-amplified tumors. They also displayed a strong tumor-associated inflammatory reaction. HER2-amplified urothelial bladder cancers therefore have somewhat specific morphological characteristics, often are HER2 protein positive, and, while mostly HER2 wild type, are occasionally HER2 mutated. Further exploration of urothelial bladder cancer seems necessary to optimally define those with a high probability of response to HER2-targeting therapy.

Miscarriage due to placental insufficiency in a context of preeclampsia remains a significant health problem, and Kim et al. ([DOI 10.1007/s00428-015-1759](https://doi.org/10.1007/s00428-015-1759)) studied relationships between placental C4d, maternal HLA antibodies, and placental pathology. They found C4d deposits on syncytiotrophoblast more frequently in preterm preeclampsia cases with fetal growth restriction than in preeclampsia patients without fetal growth restriction or in cases of spontaneous preterm delivery. There was no difference in the proportion of maternal anti-fetal HLA antibody positivity between these categories. The importance of this study is that it confirms frequent placental C4d deposition in preeclampsia with fetal growth restriction and miscarriage, which suggests that it is a consequence of defective placentation rather than a specific maternal immune response against fetal HLA. It also emphasizes the usefulness of C4d as biomarker of a placenta at risk.

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