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EDITORIAL

In this issue

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A new issue, once again a bouquet of attractive papers. First of all the paper by Droit-Dupré et al. (10.1007/s00428-015-1724-9). The group studied colonic adenocarcinomas, not otherwise specified, by immunohistochemistry for the expression of markers of intestinal epithelial cell differentiation. Hierarchical clustering analysis identified a major cluster of two thirds of the case series, expressing cytokeratin 20, CDX2 and MUC2 and invariably mismatch repair competent, which they called crypt-like. In stage III colon cancer, the crypt-like cluster had a better prognosis. The paper is a relatively simple example of what is happening in cancer classification beyond morphology: multiparameter differentiation and (epi)genomic markers defining new subtypes of cancer with potential clinical significance in clinical decision making.

The paper by Coenegrachts et al. (DOI 10.1007/s00428-015-1728-5) focuses on a remarkable example of tumor heterogeneity in endometrial cancer. The group used analysis of KRAS, PIK3CA, PTEN and TP53 as well as mismatch repair competency to study mixed endometroid and serous endometrial carcinomas. Microdissection was used to obtain tissue samples of both histotypes. Key questions were clonal origin of tumors with heterogeneous differentiation and prognostic impact of individual histotypes. Remarkably, in some cases the mutation pattern was different between the endometroid and the serous component of the same tumor, which raises the possibility of early clonal divergence or even biclonal origin. Survival of mixed endometroid and serous carcinoma was intermediate between that of pure endometroid (worse) and endometroid (better) carcinoma. The cover image on this issue is taken from this paper and strikingly illustrates dual (endometroid and serous) differentiation in an endometrial carcinoma.

Yet another example of tumor heterogeneity is the subject of the paper by Pedeutour-Braccini et al. (DOI 10.1007/s00428-014-1712-5). They noticed in a subset of cases of grade II glioma highly cellular microfoci with high vascular density and wondered whether these might be an early indicator of progression towards grade III glioma. They set out to study cell proliferation, hypoxia and vascular parameters by immunohistochemistry and fluorescence-in-situ in hypercellular foci of grade II glioma cases. Marker expression confirmed higher proliferative activity and altered microvasculature. Patients with a grade II glioma with hypercellular microfoci had shorter survival than those without. These microfoci might therefore be an early histological hallmark of progression. The authors question the discriminative capacity of the current glioma classification and argue in favor of the creation of a grade intermediate between glioma grades II and III.

Finally, in the paper by Pizem et al. (DOI 10.1007/s00428-014-1715-2) the question is asked whether the presence of pseudoangiomatous stromal hyperplasia and multinucleated stromal giant cells in gynecomastia is associated with neurofibromatosis type 1 (NF1). This peculiar morphology had been noted in NF1 patients but a systematic study of a large series of gynecomastia cases was necessary to assess whether the association is real or the result of selection bias. In a small number of a large series of gynecomastia cases pseudoangiomatous stromal hyperplasia and in even fewer cases multinucleated giant cells were found but in none of these cases an NF1 gene mutation was found by next generation sequencing. These stromal parameters are therefore not specifically associated with NF1.

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