

In this issue

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In this issue, several authors address prognostic factors in a variety of different tumors. Prognostic factors are a favorite subject for histopathologists with a desire to publish. Unfortunately, few make it to real application in clinical practice. Why we still publish these papers? Well, up front it is difficult to discern between those that will make it and those that will not. In addition, application in daily practice is not the only reason to search for associations between marker expression and prognosis. Through this panoply of marker studies knowledge is gained on new features of tumors, contributing to understanding biology or a stepping stone towards further validation. Along these lines Betge et al (DOI 10.1007/s00428-016-1970-5) studied expression of gastro-intestinal mucins (MUC1, MUC2, MUC5AC and MUC6) in colorectal cancer. Their approach was classical: immunohistochemistry on a tissue micro-array and correlation with progression-free and cancer-specific survival. It turns out that in some colorectal cancers mucin production goes ‘off-beat’: about a quarter loose expression of intestinal MUC2 while around 10% gain expression of gastric mucin (either MUC5AC or MUC6). Strikingly, loss of MUC2 was associated with poor outcome while gain of gastric mucin expression was associated with good prognosis. Mechanisms are not addressed in this paper but why some colorectal cancers convert to the production of aberrant mucins merits to be further studied.

The cover image is from this paper and shows MUC6 expression in a colorectal cancer.

An example of a marker study of which the results deepen our knowledge of the biology of a specific type of cancer is the paper by Agaimy et al (DOI 10.1007/s00428-016-1977-y). They looked at proteins involved in chromatin structure, notably the SWI/SNF chromatin remodelling complex, which might be involved in the pathogenesis of various types of undifferentiated carcinoma. Nuclear morphology remains an important parameter for cancer diagnosis and it would not come as a surprise if proteins involved in chromatin structure would be involved in such cancers. The group used antibodies against a series of SWI/SNF components to immunohistochemically stain urothelial cell carcinomas with an undifferentiated component, in search of expression patterns in association with morphological characteristics. Complete loss limited to the undifferentiated component of at least one SWI/SNF subunit was detected in a large majority of cases. Urothelial carcinoma, therefore, appears to be another tumor type in which loss of differentiation goes along with (partial) loss of expression of the SWI/SNF complex. This is, not surprisingly, accompanied by a more aggressive clinical course.

Alos et al (DOI 10.1007/s00428-016-1982-1) hypothesized that head and neck high-grade neuroendocrine carcinomas might be related to human papillomavirus (HPV) associated non-keratinizing squamous cell carcinomas in this region. They studied expression of p16, Rb and cyclinD1 as well as presence of Merkel cell polyoma virus (by immunohistochemistry) and presence of HPV (by in situ hybridization and PCR). All cases were positive for p16 while most lost Rb and cyclinD1. None of the cases presented evidence for involvement of either HPV or Merkel cell polyoma virus. The authors conclude that while neither of the studied viruses seem to be involved, p16 is strongly positive. In the head and neck region p16 staining of an undifferentiated carcinoma therefore should not be taken as solid evidence for HPV involvement.

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Shin et al (DOI [10.1007/s00428-016-1971-4](https://doi.org/10.1007/s00428-016-1971-4)) revisit an important question : is the volume of a prostate cancer associated with the likelihood of (biochemical) recurrence ? To this end they studied in patients who had undergone radical prostatectomy tumor macroscopy (volume, growth pattern and T-stage) in correlation with pre-operative imaging, Gleason score and recurrence risk. Tumor volume appeared as independent predictor of re-

currence, which is not surprising. The novelty of this paper is in the definition of a highly reproducible macroscopic (growth pattern based) classification system, which appeared to correlate well with pre-operative imaging data and seems to provide an improvement on the definition of T-stage. The latter merits to be more extensively studied before new T definitions might be envisaged in prostate cancer.