In this issue

Fred Bosman¹

© Springer-Verlag Berlin Heidelberg 2016

This issue starts with a couple of review papers on colorectal cancer. De Smedt et al. (DOI [10.1007/s00428-015-1886-5](https://doi.org/10.1007/s00428-015-1886-5)) address morphological evidence of invasive growth, a process histopathologists tend to call budding. The morphological definition is detachment of individual or small clusters of up to five tumour cells from the main tumour mass and invasion into the surrounding stroma. About one third of colorectal cancers show this feature, which has been associated with lymphovascular invasion, lymph node and distant metastasis and poor prognosis. Two important issues are addressed. Firstly, for a morphological parameter to be used as a biomarker it needs to be quantified. Generally accepted and reproducible approaches for semi-quantitative assessment of budding are lacking, however, which hampers the use of this parameter in clinical practice. Secondly, mechanisms involved need to be unravelled in detail. Budding in all likelihood is associated with epithelial-mesenchymal transition and the stromal response to invasive cells. Understanding the details might provide better parameters to assess budding. The paper presents an overview of tumour budding including its definition, scoring systems, prognostic relevance and biological mechanisms involved.

The paper by Polonia et al. (DOI [10.1007/s00428-016-1903-3](https://doi.org/10.1007/s00428-016-1903-3)) presents an interesting example of how changing guidelines might lead to shifts in selection criteria of patients for treatment. They compared results of HER2 testing of breast cancer using the 2007 ASCO/CAP criteria with those using the 2013 guideline. They applied the standard immunohistochemical staining and for HER2 amplification assessment by in situ hybridization with silver chromogenic development. The good news is that the proportion of HER2-equivocal cases was significantly reduced. This, however, went along with an increase in the proportion of HER2-positive cases which reached beyond 50 %. Important follow-up information needs to be collected in such a situation:

do the ‘new’ HER2 positive cases respond equally well to anti-HER2 targeted therapy than the ‘conventional’ HER2 positive cases? The paper does not explicitly address this issue but hopefully studies are under way to provide an answer to this question.

In the paper of Pelosi et al. (DOI [10.1007/s00428-016-1906-0](https://doi.org/10.1007/s00428-016-1906-0)) the question is raised whether or not DNA retrieved from tissue sections that has been H&E or immunohistochemically stained and stored can be used for molecular testing. They used as methods fluorescence in situ hybridization (FISH) with a variety of probes as well as Sanger or targeted next generation sequencing for detection of *BRAF*, *EGFR*, *KRAS*, *C-KIT* and *TP53*. It turns out that for FISH almost perfect concordance is reached between test results obtained on pre-stained sections. For immunohistochemically stained sections there was no difference between alkaline phosphatase or peroxidase as label. When sequencing was performed on sections with negative immunohistochemical results the concordance with fresh unstained sections was perfect. For immunohistochemical stains with nuclear reactivity concordance dropped to about 50 %. The conclusion is that stained sections are a valuable resource for FISH or sequencing analysis when no other tissue sample is available, but on cases expressing nuclear markers cautious interpretation is called for. The image on the cover shows a FISH result from this paper.

Finally Cerni et al. (DOI [10.1007/s00428-016-1909-x](https://doi.org/10.1007/s00428-016-1909-x)) address the question how reliable micro-invasion in in situ breast cancer can be assessed. The distinction between in situ carcinoma and micro-invasive carcinoma is of clinical significance as it impacts on clinical staging with therapy implications. The authors requested a sizeable group of dedicated breast pathologists to make this call on H&E stained digitized images using predefined criteria. After a ‘wash-out’ period the same group was requested to make the call using additional slides immunohistochemically stained for myoepithelial cells. It is not surprising that consistency in the recognition of microinvasion significantly improved with the use of myoepithelial markers, which corroborates previous recommendations to use myoepithelial markers in case of uncertainty exists about the presence of micro-invasion. When doubt remains, a second-opinion by an independent pathologist is advocated.

✉ Fred Bosman
fred.bosman@citycable.ch

¹ University Institute of Pathology, Lausanne University Medical Center, Lausanne, Switzerland