In this issue

Fred T. Bosman¹

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This month's issue opens with a new element in the papers our Journal publishes; let us call it miniseries. Some topics need more space to be dealt with in a comprehensive and didactic way, but do not merit a full review issue. Miniseries will be authored by recognized experts in the field on topics of common interest in diagnostic histopathology and published at regular intervals. Along this line, Den Bakker et al. (DOI [10.1007/s00428-015-1830-8](https://doi.org/10.1007/s00428-015-1830-8) and [10.1007/s00428-015-1832-6](https://doi.org/10.1007/s00428-015-1832-6)) comprehensively discuss soft tissue tumors of the mediastinum, based upon the 2013 WHO classification of soft tissue tumors and the 2015 WHO classification of tumors of the lung, pleura, thymus and heart. Most of us will not see these often, but for the general diagnostic histopathologist, it is important to be aware of common and less common entities one might encounter there.

The cover image is from one of these papers and shows a membranous CD31 expression pattern in an epithelioid hemangioendothelioma.

Grading of neuroendocrine tumors (NET) has been a hotly debated issue for a long time, and proliferative activity, as reflected in the Ki67 index, has become a cornerstone in the currently used grading approach. And yet, controversial issues remain, including inter-observer reproducibility, whether or not automated counting might improve its assessment and what the most appropriate cutoff might be. Blank et al. (DOI [10.1007/s00428-015-1843-3](https://doi.org/10.1007/s00428-015-1843-3)) address inter-laboratory reproducibility, in particular for cases with a low proliferative index which discriminates between grade 1 and grade 2 NET. Ki67 staining of a cohort of these tumors was performed in three different pathology laboratories, labeling indices were

determined and mitotic counts were recorded. It turns out that, even though overall moderate-to-fair agreement was found, in the low-range counts, significant inter-laboratory differences occur. The authors conclude that external quality control is called for.

Chronic obstructive pulmonary disease (COPD) is a very prevalent condition, and most of us have been or are regularly confronted with bronchial biopsies with a question: is this a case of asthma or is this COPD? Can this distinction really be made? Ten Hacken et al. (DOI [10.1007/s00428-015-1824-6](https://doi.org/10.1007/s00428-015-1824-6)) tackle this issue on a well-defined cohort (matched for smoking history, age and corticosteroid use). General and expert pulmonary pathologists assessed online virtual slides without upfront clinical information. The authors found clinically concordant diagnoses of asthma or COPD in about 60 % of the cases. General and pulmonary pathologists did equally well. The younger the patients were, the better concordance was. Along the line, the authors provide practical hints to help solve this regularly difficult differential diagnosis. What transpires is that differentiation between asthma and COPD by histopathology is difficult without relevant clinical information.

Geurts Giele et al. (DOI [10.1007/s00428-015-1817-5](https://doi.org/10.1007/s00428-015-1817-5)) address the interesting question how to distinguish, in patients with multiple tumors, between metastatic disease and multiple independent primary tumors. Often morphology and detailed clinical information will do but this can be a real challenge, notably as the provided diagnosis might affect prognosis and treatment decisions. The authors chose to study tumor clonality by assessing mutations in mitochondrial DNA. They found somatic mutations of the D310 mononucleotide in several tumor types and overall in about one in four cases. Results of clonality analysis were mostly corroborated by Sanger sequencing of genomic DNA. This might become a new way to assess clonality for a subgroup of tumors, and the authors propose to complement next generation sequencing targeted genomic DNA assays with mitochondrial DNA markers.

✉ Fred T. Bosman
fred.bosman@citycable.ch

¹ Institute of Pathology, University Medical Center (CHUV) of Lausanne, Lausanne, Switzerland