

In this issue

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What should catch the eye in this issue? Mammary analogue secretory carcinoma (MASC) of the salivary gland is certainly worth to spend some time on. Majewska and collaborators (DOI [10.1007/s00428-014-1701-8](https://doi.org/10.1007/s00428-014-1701-8)) describe a series of new cases of this recently defined entity, which is characterized at molecular level by the ETV6-NTRK3 translocation. By careful morphological evaluation and application of immunohistochemistry, fluorescence in situ hybridization (FISH) for ETV6 rearrangement, and RT-PCR for detection of the ETV6-NTRK3 fusion transcript, seven cases were identified out of a historical series of over 180 salivary gland carcinomas. The paper describes morphology and immunophenotype and concludes that this entity might not be as rare as originally assumed. It was not included in the 2005 Edition of the WHO classification of Head and Neck Tumors and certainly deserves to be included in the upcoming next edition. MASC shares morphological features with other malignant salivary tumors, and awareness of its characteristic features will help to better define its incidence and clinical behavior.

The paper by Yoshiko and coworkers (DOI [10.1007/s00428-014-1705-4](https://doi.org/10.1007/s00428-014-1705-4)) addresses the issue of the histopathological diagnosis of biliary tract lesions, notably on small endobiliary biopsy specimens. They used a detection series of surgical specimens to test sensitivity and specificity in distinguishing between neoplastic and non-neoplastic epithelium. As markers, they chose claudin-18, a tight junction protein with a high level of tissue specificity, maspin, a member of the serpin family of serine protease inhibitors, and good old p53 to attain over 90 % sensitivity and 100 % specificity. They then validated the panel on small endobiliary forceps biopsies to get to almost the same level of sensitivity and specificity.

This panel might well provide useful support in the diagnostic work-up of such cases.

The mechanisms involved in the astonishing multifocality of papillary urothelial carcinoma were studied in a single case by Warrick and collaborators (DOI [10.1007/s00428-014-1699-y](https://doi.org/10.1007/s00428-014-1699-y)). They used next-generation sequencing to examine in detail the molecular characteristics of five spatially distinct urothelial cell carcinomas in a single patient. Of the nine somatic mutations found across the five different samples, all lesions had five in common, which confirms the common clonal origin of all five lesions. The tumor sample taken from the single site of invasive urothelial cancer furthermore showed unique molecular characteristics, which were also found in an additional case set of invasive urothelial cancers. The paper shows how well-designed single-case studies, eventually completed by small selected case series to validate the findings, may contribute new elements to our growing insight in tumor heterogeneity. The cover image is from this paper and shows mutant allele frequencies, according to a color scale, in the different tumor samples studied.

Taube and coworkers (DOI [10.1007/s00428-014-1710-7](https://doi.org/10.1007/s00428-014-1710-7)) report on neuroendocrine differentiation in high-grade serous ovarian carcinoma. They applied a tissue micro-array strategy to study a large series of these lesions by immunohistochemistry, using the classical markers chromogranin and synaptophysin. As has been found in a variety of different organ sites, expression of these markers occurred in between 7 and 20 % of the tumors. Of note, in some lymph node metastases, neuroendocrine cells dominated, which provides evidence of the neoplastic nature of the neuroendocrine cells and also of the (microenvironment-related?) phenotypical plasticity of tumor cells. The authors furthermore found that expression of synaptophysin and less so of chromogranin is associated with poor prognosis. Time will tell if these markers identify a subgroup of patients for whom a more specific therapeutic approach might be developed.

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