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NEWS

In this issue

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The content of this month's issue once again illustrates the focus of our Journal: diagnostic pathology with an emphasis on new molecular diagnostics and applying insight in molecular mechanisms for classification, as well as on education in pathology. To begin with the latter, Egevad et al. (https://doi.org/10.1007/s00428-019-02540-w) report on the efforts of the International Society of Urological Pathology (ISUP) to improve diagnostic performance regarding histological classification of neoplastic lesions in the prostate using web-based education tools, including tutorials and formative tests. The paper presents two remarkable results. First is documentation of the differences in performance between pathologists from upper middle, lower middle and low resource countries in Asia and South America, those from low resource countries reaching a correct diagnosis before the teaching course in less than half of the cases, while upper middle and lower middle income country based pathologists were correct in roughly two out of three cases. The second is the efficacy of the web-based education tools: low resource country-based pathologists came close to the performance of those from (upper and lower) middle income countries after taking the course. The results emphasize the importance of web-based teaching, limited in the paper to pathologists based in countries with low resources but undoubtedly valid also for pathology training in high resource countries.

In the realm of applied molecular pathology Baretton et al. (https://doi.org/10.1007/s00428-019-02541-9) report on the performance of HER2 testing in metastatic gastric or gastroesophageal junction cancer in 50 pathology centres in Germany. As accurate identification of patients with a HER2-positive cancer is essential for effective targeted treatment, optimal testing is crucial, and the paper shows how monitoring of performance of participating institutions in combination with analysis of patient, tumor, pre-analytical and analytical factors can contribute to improvement in the quality of molecular testing. The paper by Schmoeckel et al. (https://doi.org/10.1007/s00428-019-02528-6) has a somewhat similar focus. Given the paucity of strategies for targeted treatment of ovarian cancer the group applied immunohistochemical (for PD-L1, HER2, ALK and the mismatch repair proteins MLH1, PMS2, MSH2 and MSH6) and fluorescence in situ hybridization (for HER2 amplification and ALK/EML4 fusion) testing to a cohort of ovarian carcinomas, with the intention to identify subgroups potentially amenable to therapies targeting these molecular events. PD-L1 expression was found in about one in five patients, suggesting that immune-checkpoint blocking therapy might be considered for such cases. HER2 amplification was found in a small number of cases whereas ALK/EL4 fusion and mismatch repair deficiency was very rare. One might argue that when a particular event is rare in a tumor type, its testing is not relevant. This may be true at a population level but for the patient whose cancer is characterized by such a rare targetable event, the possibility of targeted treatment can be quite relevant. We may end up with the conclusion that cancers considered as frequent in fact represent a collection of rare (potentially treatable) molecular subtypes. How The Cancer Genome Atlas (TCGA) data can be used to develop molecular profiles useful in cancer classification is illustrated in the paper by Cuevas et al. (https://doi.org/10.1007/s00428-018-02516-2). Given the difficulties in correctly differentiating between endometrioid and serous endometrial carcinomas, they set out to identify a panel of molecular markers that might distinguish between the two. The TCGA database was used to identify genes often mutated in endometrial carcinoma. It turns out that a panel of six genes (ARID1A, PIK3CA, PTEN, PPP2R1A, KMT2B and TP53) allowed correct classification of all cases, using histology as gold standard. This is quite promising, but the studied case series is quite small and application in daily practice will await validation through a prospective study on a large series of cases. A somewhat similar approach is taken by Wijvekens et al. (https://doi.org/10.1007/s00428-019-02526-8), who discuss how to subclassify the recently WHO canonized microphthalmia transcription factor (MiT) family of translocation renal cell carcinomas. We rarely highlight case reports, but this report has an important message, based on two cases of renal cancer with an aberration in the gene encoding the transcription factor EB (TFEB), belonging to the MiT family. The TFEB gene can be involved in a chromosomal translocation but can also be

amplified. The (morphological and molecular) pathological characteristics and clinical behaviour differ between TFEB translocated and TFEB amplified cases and the report of these two cases allowed the authors to discuss how these two categories can be distinguished.

Finally, the paper by Keelawat and Bychkov (https://doi.org/10.1007/s00428-019-02536-6) sheds some light on the origin of C-cells in the thyroid. The classical hypothesis is that C-cells arrive in the developing thyroid through migration of precursor neuroendocrine cells from the neural crest. A more recent hypothesis is that C cells may be derived from progenitor cells of the midline thyroid primordium. The authors characterized in detail the cell types present in a series of thyroglossal duct cysts, including lining epithelium and thyroid remnants, more specifically looking for neuroendocrine cells. Thyroid remnants showed immunoreactivity for thyroid specific markers, but calcitonin expression was not found. In contrast, cyst lining epithelium was of the respiratory epithelium type and contained neuroendocrine cells, some of which expressed calcitonin. The authors hypothesize that the latter might be the potential source of medullary carcinoma-like neuroendocrine tumors in derivatives from the median anlage. They do not reflect in detail on the origin of thyroid C-cells, but the findings do not contradict the classical hypothesis.

The cover image is from this paper and illustrates the author's concept of compact epithelial buds in thyroglossal duct cysts with dual immunophenotype and how they evolve.