Title: Multi-model assessment of tumor budding

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Abstract: Tumor budding is recognized as an important prognostic feature across numerous solid cancers. Molecular, immunohistochemical and imaging data suggest that a subpopulation of tumor budding cells is in a state of hybrid Epithelial-Mesenchymal Transition (EMT), which contributes to increased vessel invasion, metastasis and possible therapy resistance. The diagnostic reporting of tumor buds is now also included in key pathological (e.g. CAP) and oncological (e.g. ESMO) guidelines.

The International Tumor Budding Consensus Conference (ITBCC) guidelines recommend a three-tier method for tumor bud assessment based on counts of individual buds in a hotspot of 0.785 mm2 on an H&E slide. Although developed for colorectal cancers, the method has been validated across various tumor entities, but is not without its challenges.

Automated scoring of tumor buds is proposed as a possible solution to help reduce inter-observer variability (e.g. selection of hotspots and budding counts) and render the task less daunting. A dozen open-source and commercially available algorithms offer tumor bud assessment, but most notably vary with regards to staining method for algorithm development (immunohistochemistry, immunofluorescence or H&E).

Here, we will discuss the challenges in building such algorithms for budding detection and the practical aspects for real-life integration.

Finally, we will look upon future possibilities for integrating morphology with spatial profiling using high-dimensional (multiplexing) protein analysis to further unravel the complex interactions of the tumor budding microenvironment.