this study was to evaluate RKIP expression and to determine its association with clinicopathological features, including EMT in form of tumor budding in pancreatic ductal adenocarcinoma (PDAC).
Methods. Staining for RKIP was performed on a multipunch Tissue Microarray (TMA) of 120 well-characterized PDACs with clinicopathological, follow-up and adjuvant therapy information. RKIP-expression was assessed separately in the main tumor body and in the tumor buds. Another 3 TMAs containing normal pancreatic tissue, precursor lesions (Pancreatic Intraepithelial Neoplasia, PanINs) and matched lymph node metastases were stained in parallel. Cut-off values were calculated by receiver operating characteristic (ROC) curve analysis.
Results. We found a significant progressive loss of RKIP expression between normal pancreatic ductal epithelia (average: 74%), precursor lesions (PanINs; average: 37%), PDAC (average: 20%) and lymph node metastases (average: 8%, p<0.0001). RKIP expression was significantly lower in tumor buds (average: 6%) compared to the main tumor body (average: 20%, p<0.005). RKIP loss in the tumor body was associated with higher tumor grade (p=0.0389), increased T-stage (p=0.045) as well as high-grade peritumoral (p=0.0051) and intratumoral budding (p=0.0227). RKIP loss in the buds was associated with increased T stage (p=0.0091) and showed a trend towards worse patient survival (p=0.0763).
Conclusions. The progressive loss of RKIP seems to play a major role in the neoplastic transformation of pancreas and correlates with aggressive features in PDAC, especially characterized by the presence of EMT in form of tumor budding.

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FP33
Intratumoural budding (ITB) in preoperative biopsies predicts the presence of lymph node and distant metastases in colon and rectal cancer patients

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Background. In the inter-disciplinary pre-operative management of colorectal cancer patients, the pathologist's role is limited to a confirmation of malignancy from the biopsy; other relevant histomorphological parameters apply only to the surgical resection. Tumour budding (the presence of detached tumour cells) has consistently been associated across studies with lymph node (LN) and distant metastasis. Interestingly, tumour budding can also be detected in biopsies (intra-tumoural budding; ITB) and may have similar clinical importance. The aim of this study was to investigate whether ITB in pre-operative colon and rectal cancer biopsies can be translated into daily diagnostic practice.
Methods. Pre-operative biopsies from 152 patients with primary colorectal cancer underwent immunohistochemistry for AE1/AE3 to facilitate visualization of tumour buds. All biopsies from each patient were evaluated; the region containing the densest number of buds was identified. All buds in this "hot-spot" were counted at 40× (high-power field, HPF).
Results. In non-neoadjuvantly treated patients, a greater number of tumour buds in the biopsy was associated with pT stage (p=0.0143), LN metastasis (p=0.0007), lymphatic (p=0.0065) and venous vessel invasion (p=0.0318) and distant metastasis (cM1; p=0.0013). Using the logistic regression equation, a probability "scale" was developed to estimate the probability of LN and distant metastasis using the number of tumour buds (e.g. 30 buds/HPF: 86% chance of LN metastasis). Although only 19 patients received neoadjuvant therapy, a greater number of tumour buds in the pre-treatment biopsy was related to lymphatic invasion (p=0.0337). The marginal significance for pT (p=0.0623) and tumour regression grade (p=0.0778) requires confirmation on a larger cohort. The interobserver agreement was excellent (ICC: 0.813).
Conclusions. Tumour budding can be assessed in the preoperative biopsy of colon and rectal cancer patients. It is practical to evaluate, reproducible and predictive of LN and distant metastasis. ITB qualifies for further investigation in the prospective setting.

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FP34
TrkB expression in colorectal cancers highlights anoikis-resistance as a possible survival mechanism of tumor budding (EMT-like) cells

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Background. Tumour buds in colorectal cancer represent an aggressive subgroup of non-proliferating and non-apoptotic tumour cells. We hypothesize that survival of tumour buds is dependent on resistance to anoikis (cell death due to detachment from the extracellular matrix). Here we investigate the role of neurotrophic tyrosine kinase receptor TrkB, a promoter of epithelial-mesenchymal transition (EMT) and anoikis-resistance, in facilitating a pro-tumour budding phenotype.
Methods. TrkB immunohistochemistry was performed on a multiple-punch tissue microarray of 211 colorectal cancer patients. Cytoplasmic (cTrkB) and nuclear (nTrkB) staining were evaluated in tumour and tumour buds. KRAS/BRAF mutations were investigated.
Results. cTrkB and nTrkB were strongly inversely correlated in tumour (r=−0.38; p<0.0001) and tumour buds (r=−0.41; p<0.0001). cTrkB was associated with high-grade tumour budding (p<0.0001), KRAS mutation (p=0.0008) and expressed frequently in tumour buds (100/154 cases; p<0.0001). In low-grade budding cases, cTrkB was significantly associated with lymph node positivity (p=0.0555) and venous invasion (p=0.0394) with marginal significance for lymphatic invasion (p=0.0879), after adjusting for adjuvant therapy. cTrkB positive tumours (p=0.049) and those with positive