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MODERN PATHOLOGY

Differential testing of two approved PDL1 assays

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Identifying a biomarker as a potential diagnostic tool is only the beginning; the next step is the evaluation and validation of its usefulness in testing. Reisenbichler et al. compared SP142 and SP263 assays and interpreted the percentage and immune cell (IC) staining by 19 pathologists across 14 academic institutions, utilizing a method they call ONEST (“observers needed to evaluate subjective tests”) to ascertain the minimum number of evaluators needed to estimate concordance. By identifying IC and concordance between cases, the SP142 assay was determined to be inferior to the SP263 assay in interpreting PDL1 positivity. Using ONEST plots, the authors found that more observers were needed to reach agreement using SP263 compared with SP142, and that IC detection was often difficult to reproduce—the analysis suggested that more than half of pathologists will disagree about IC scores. The US Food and Drug Administration has approved SP142 for determining eligibility for atezolizumab therapy, but these data indicate that patients might be receiving the treatment who are not likely to benefit, whereas others who might benefit are not receiving the treatment.

Virtual IHC could save tissue, time, and money in cancer diagnostics

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Immunohistochemistry (IHC) is a widely used diagnostic technique, but it can be costly and demanding because of the

amount of tissue needed. Jackson et al. proposed a machine-learning algorithm that would enable the use of simple hematoxylin and eosin (H&E) staining to provide the same data. The group performed H&E staining on 12 slides and registered images before destaining, and then performed IHC for SOX10 and registered a second set of images. The two images for each sample were compared, and color-thresholding and machine learning techniques were employed to identify 3,396,668 SOX10-negative cells and 306,166 SOX10-positive cells, which became the basis for a convolutional neural network trained to predict SOX10 nuclear staining. The resulting virtual IHC neural network achieved an area under the curve of 0.9422 in an analysis of receiver operator characteristics when sorting individual nuclei. The authors note that more work is needed but that this technology could have a wide-ranging impact on the diagnosis and treatment of cancer patients.

LABORATORY INVESTIGATION

Nervous system—specific NRBF2 KO results in memory and learning deficits

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Ouyang et al. explored the role of nuclear receptor-binding factor-2 (NRBF2) in learning and memory. The group hypothesized that NRBF2 deficiency plays a role in cognitive deficits. They developed a mouse model with a specific nervous system knockout (KO) of NRBF2 that resulted in profound learning and memory deficits without impact to motor coordination; the mice were able to spend as much time as wild-type controls on a rotarod but had longer escape latencies. RNAseq analyses showed altered expression of genes that have been shown to impact neuronal function. NRBF2 modulates transcriptional activities of retinoic acid receptor α and retinoid X receptor α , and the autophagic activities of