Letters to the Editor

Immunohistochemical Localization of RPA-1; Comment on Paper by Zhang et al., *Toxicol Pathol* 36;397

The field of biomarkers of efficacy and toxicity is undergoing rapid growth, and a wide range of novel antigens is being evaluated once antibody reagents become available. In addition to analytical and biological evaluation in appropriate biofluids (plasma, urine, CSF, etc.), it is important to anchor the biomarker to a specific pathology and site of tissue expression. Immunohistochemistry provides persuasive evidence for cell and tissue specificity as site of origin of a novel biomarker prior to entry into biofluids. The recent paper by Zhang et al. (*Toxicol Pathol* 36;397) dramatically demonstrates cell type specificity with the example of RPA-1, a rat collecting duct marker (see front cover of volume 36, issue number 3). The authors claim additional induction of RPA-1 expression in cortical proximal tubules by IHC following gentamycin treatment (see Figure 3). However, closer inspection of the images showing the “enhanced S1/S2 segment expression” reveals that the stained cells are clearly necrotic. The IHC methods employed omission of the primary antibody as the negative control because the correct isotype control was not available from the antibody vendor, despite other mouse control IgGs being available from other vendors. In my experience, any novel IHC method must include relevant controls being conducted prior to publication so that misleading observations, for example, false-positive staining of necrotic cells, do not confound studies on novel biomarkers. RPA-1 is an excellent collecting duct injury marker in the rat, but I am not persuaded that it can be induced in the proximal tubule of the kidney based on the published evidence.

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