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Letter to the Editor

Tissue microarrays, tread carefully

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To the editor: Tissue microarrays (TMAs) have provided a significant technological advance for evaluating and validating antibodies for immunohistochemistry as well as clinical biomarker development. As with any new method, there are always concerns that need to be addressed prior to widespread acceptance of the technique. In a key study, Camp *et al* showed that antigenicity is preserved in long-term stored blocks and that they are suitable for constructing TMAs. They also demonstrated the need for redundancy to ensure proper sampling of the tissue.[1] DiVito *et al*.[2] have taken this a step further by showing that prepared TMA slides need to be stored properly in order to prevent the loss of antigenicity.

We have also made an observation that we feel is noteworthy in light of the increased use of TMAs. We recently completed a study (Mikhail *et al*, manuscript in preparation; same cohort was used previously in Harzan *et al*[3]) examining *PTEN* expression in formalin-fixed paraffin-embedded whole section skin/melanoma specimens. Out of 150 section slides tested (dating back to the mid-1970s), 16 did not show any labeling in the tumor or normal epidermis. We noticed that the unmelted paraffin wax in this subgroup of slides (from the early 1980s) had a distinctly different appearance than the others in the group. Under polarized light, the paraffin crystals were large and tetragonal-like. They ranged in size, from 10 to 50 μm (longest dimension at $\times 20$) and were haphazardly arranged. In contrast, the paraffin of the other samples consisted of small hexagonal-like crystals, measuring approximately 10 μm. They were uniformly and regularly arranged. The tetragonal-shaped paraffin wax did not melt at the regular incubation temperature of 60°C; but did at approximately 80°C. After incubating at the higher temperature, 14 out of the 16 samples that did not label previously showed labeling in both tumor and normal epidermis. In addition, our staining protocol requires heat induced antigen retrieval ($\sim$99°C) in 0.01 M citrate for 20 min in a 1200 W microwave oven. Interestingly, antigen retrieval did not initially 'unmask' the antigen in these samples; only melting at the higher temperature followed by antigen retrieval induced immunoreactivity.

This observation suggests that it is still important to take into consideration the source of the tissue blocks when constructing TMAs so that false positives and negatives are minimized. This is essential if multi-institutional studies are performed where tissues may be collected from several different hospitals. We commend Camp and DeVito for their efforts in addressing important issues in the use of TMAs.

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