Cytoplasmic MUC1 in PanIN-1

To the Editors: In a recent issue of Clinical Cancer Research, Dr. Gold describes MUC1 as a biomarker of pancreatic intraepithelial neoplasm of low grade (PanIN-1) using PAM4 monoclonal antibodies (mAb; ref. 1). This claim is questionable.

PAM4 mAb does not react in normal pancreas, but several articles describing the use of immunohistochemistry, Northern blotting, and in situ hybridization show that MUC1 is located in epithelial cell membranes (apical pole; ref. 2). At the TD-4 San Diego workshop of the International Society for Oncodevelopmental Biology and Medicine, it was shown that 53 of 56 anti-MUC1 mAbs showed apical membrane staining, and the remaining 3 mAbs that displayed a cytoplasmic staining were regarded as having an “obscure specificity” (probably non MUC-1; ref. 3). The PAM4 mAb was not submitted to this international workshop. The MUC1 immunoreactivity of PAM4 mAb has never been tested on the MUC1 peptide. MUC1, initially defined as mammary type mucin, is a biomarker of breast adenocarcinoma. PAM4 mAb does not immunoreact with these tumors. Dr. Gold’s work shows specific cytoplasmic expression of MUC1 in PanIN-1. Other works show that MUC1 loses its apical distribution in favor of a cytoplasmic staining in PanIN-3 and in ductal adenocarcinoma. This change is regarded as a pertinent biomarker of malignancy (4).

In fact, PAM4 mAb could be an anti-MUC5AC because it displays a secretory cytoplasmic staining as do most anti-secreted MUC mAbs. PAM4 is restricted to the gastric epithelium similar to MUC5AC. In the PanIN, the PAM4 mAb strongly stained the mucus cells as we have previously observed using our anti-M1/MUC5AC antibodies in pancreatic gastric hyperplasia (5), now called PanIN. In carcinomas, the PAM4 expression pattern is similar to that of the MUC5AC mucin (6). Using ELISA, Dr. Gold showed MUC5AC immunoreactivity in PAM4 mucin. We think that it will be important to test the immunoreactivity of PAM4 mAb against recombinant MUC5AC apomucin.

Finally, cytoplasmic MUC1 is associated with advanced stages of malignant transformation (PanIN-3). It is not acceptable to claim that cytoplasmic MUC1 is a biomarker for early pancreatic carcinogenesis (PanIN-1). A working hypothesis should be that PAM4 is an anti-MUC5AC.

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References

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No potential conflicts of interest were disclosed.
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