We read with great interest the recent article of Moinova and co-workers reporting that aberrant methylation of exon-1 of the vimentin (VIM) gene is a highly common epigenetic alteration in neoplasia of the upper (esophagus and gastric) and the lower (colorectal) gastrointestinal tract (1).

We have recently analyzed the methylation of VIM by quantitative methylation specific PCR (forward primer, GGTCGAGTTTTAGTCGGAGTTACGT; reverse primer, CCCGAAAAACGAAACGTAAAAACTA; probe, 6FAM-CGTATTTATAGTTTGGGTAGCGC-MGB; modified from (2)) in a wide range of cell lines (n=95) originating from 17 different cancer types. The data confirmed that the VIM gene was methylated in 75% of gastrointestinal cancer cell lines (including bile duct 5/6, colon 22/25, gall bladder 1/2, gastric 4/5, liver 4/4, and pancreas 0/6).
Moinova and co-workers suggest that false positives from the VIM colorectal cancer test might be explained by the presence of neoplasia in the upper gastrointestinal tract. In this sense, feces represent an appropriate test material since the source of detected aberrant VIM methylation most likely would be restricted to cancers located in the gastrointestinal tract. In contrast, using a blood based colorectal cancer test, the number of sources for potential false positive results would increase significantly and could subsequently negatively affect the specificity of the test. Indeed, in the present study we have detected high methylation frequencies of VIM also in breast cancer cell lines (75%), as well as in cell lines from the uterus (50%). Furthermore, we observed methylation in 75% of bladder cancer cell lines, in agreement with our recent findings in urine DNA from bladder cancer patients (3).

A handful genes have so far been shown to be frequently inactivated by methylation in the majority of tumor types (4). It seems that VIM belongs to an intermediate group of genes, being methylated in a restricted number of malignancies. Several of the cell lines analyzed here, representing various cancer types, were indeed unmethylated for VIM, including altogether 22 cell lines from cancers of the kidney, lung, peripheral nerve sheath, ovary, and pancreas.

The frequent methylation of VIM previously shown for some cancer types and the overall widespread methylation of this gene across a number of cell lines from many cancer types shown in the present study, suggest feces as an appropriate material for an aberrant VIM methylation based non-invasive test for colorectal cancer to avoid too many false positives.

References

