Re: Serum miR-21 as a Diagnostic and Prognostic Biomarker in Colorectal Cancer

Toiyama et al. have demonstrated for the first time that high levels of miR-21, not only in colorectal cancer (CRC) tissues but also in serum, are associated with tumor size, distant metastasis, and poor survival (1). This report is elegant and meaningful in that the authors found “serum” miR-21 as a promising biomarker for CRC, which enables noninvasive detection and evaluation of CRC.

There are three issues we would like to address.

First, although the authors determined miR-21 expression levels in serum samples (1), it would be interesting to investigate whether miR-21 derived from exosomes (2) would also act as a diagnostic biomarker for CRC when isolated from peripheral blood. As shown by the authors (1), miR-21 is a secreted miRNA. Actually, tumors actively release exosomes into peripheral circulation, and circulating exosomes can be collected and isolated. Serum-derived miR-21 reflects total amounts of secreted miR-21, whereas “purified” exosome-derived miR-21 reflects only a part of it (3). Interestingly, Taylor et al. elegantly demonstrated that tumor-derived exosomes are useful as diagnostic biomarkers of ovarian cancer (4). In CRC, it would be valuable to determine which would be more closely associated with tumor progression, serum-derived miR-21 or exosome-derived miR-21.

Second, postoperative reductions in serum miR-21 levels occurred exclusively among patients with potentially curative surgeries (1). Because chemotherapy was administered to patients with stage III/IV disease in the study (1), it would be interesting to examine whether there were postchemotherapy reductions in serum miR-21, reflecting responsiveness to chemotherapy. Furthermore, regardless of chemotherapy, ascertaining whether serum miR-21 would serve as a long-term follow-up biomarker (like tumor marker) would be of interest.

Finally, as speculated in the accompanying editorial by Stintzing and Lenz (5), miR-21 serum levels might be elevated in CRC as a sign of an inflammatory process of adjacent healthy tissues. If this hypothesis were true, is there any evidence that postmedication reductions in serum miR-21 levels occurred in patients who received administration of anti-inflammatory drugs, such as steroids or nonsteroidal anti-inflammatory drugs (NSAIDs)? Because NSAIDs have been shown to play a role in disease prevention in CRC (6,7), further elucidation on the putative relationship between miR-21 and NSAIDs might be useful.

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References

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