Author reply

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Published online: 2 May 2011
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In their letter, Spiliotis and Zoras seem to misunderstand our position. It was never our belief that blood levels of epidermal growth factor (EGF) should be aggressively pursued as a clinical biomarker. The main purpose of our study “minimally invasive colorectal resection (MICR) associated with a rapid and sustained decrease in plasma levels of epidermal growth factor (EGF) in the colon cancer setting” was to determine the impact of MICR on postoperative plasma EGF levels in cancer patients.

As stated in the introduction to our report, it has been noted recently that plasma levels of the proteins vascular endothelial growth factor (VEGF) and angiotensin 2 (ANG2) are elevated for 2–4 weeks after MICR in the cancer setting and that, *in vitro*, plasma from weeks 2 and 3 after surgery stimulate endothelial cell proliferation, migration, and invasion versus the results obtained with preoperative plasma from the same patients.

We have been searching for other proteins that may contribute to the proangiogenic makeup of the plasma after MICR. Thus, we carried out this EGF study. The results of this study, however, imply the opposite: the EGF results suggest that angiogenesis might be transiently inhibited for several days after surgery.

In the course of this study, we also measured preoperative EGF levels in a group of patients with benign disease ($n = 40$), comparing the results with those of the cancer group ($n = 48$). The latter were noted to be significantly higher (122.9 vs 85.3 pg/ml; $p = 0.015$).

In our discussion of these findings, we noted that it was premature to declare that a true difference existed based on a combined sample size of only 88 patients. We noted that

larger studies are required for a definitive statement to be made. We concluded that “if the magnitude of the difference noted between cancer and tumor-free patients holds up and if EGF levels in cancer patients indeed return to the lower level noted in tumor-free patients or an association between disease severity and EGF level is found, then EGF may hold modest promise as a tumor marker and/or prognostic indicator.” This is hardly a strong endorsement of EGF as a tumor marker. We agree that cancer genome analysis is likely to be more successful in identifying promising tumor markers.

Finally, regarding the suggestion of Spiliotis and Zoras that we compare EGF levels after open and laparoscopic MICR for cancer, we do not agree. The various randomized trials comparing open and closed methods have shown no difference in the survival or recurrence rates between laparoscopic and open surgery [1, 2]. It is our unsubstantiated belief, at least with regard to the surgery-related persistent proangiogenic plasma protein changes, that open and minimally invasive surgical methods have similar effects. We thank Spiliotis and Zoras for their comments.

References

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