Response

We appreciate the comments by Ortolan et al. concerning our editorial on their article in the Journal. We agree that structural homologies are the weakest evidence for functional similarities. Although the extracellular domains of these CD157 and CD38 are highly conserved (having been derived from a gene duplication that placed the loci in tandem head-to-head location on chromosome 4 in humans; (1)), Ortolan et al. describe important structural distinctions between CD157 and the closely related CD38. CD157 is anchored to the plasma membrane by a glycosylphosphatidylinositol moiety, as opposed to the transmembrane hydrophobic region of the CD38 protein. These authors and others have demonstrated a clear interaction between CD38 on cells of the immune system and CD31, expressed on vascular endothelium. Interestingly, earlier work by these authors suggested a functional interplay between CD157 and CD31 since antibody blockade of either molecule resulted in nearly identical inhibition of neutrophil diapedesis across endothelial cells (2). Yet, as stated in their letter, they have not been able to show the same clarity of interaction between CD157 and CD31 in vitro, despite extensive efforts to do so. We appreciate their sharing unpublished results.

We return to the conclusion of our editorial, which is that many truly substantive studies frequently raise more questions than they answer. The negative data for a CD157–CD31 interaction leaves us with more questions: Is the lack of interaction an artifact of in vitro assay systems and is it possible that the interaction requires other cofactors not present in those assays? Or as the authors suggest, is there a different ligand? It is indeed possible that this interaction involves endothelial cell proteins other than CD31; it is also possible that the expression patterns of such ligand(s) would differ between tumor vasculature and inflammatory or immune vasculature (3). This may address a key point in developing tumor-specific antagonistic antibodies for the treatment of epithelial ovarian cancer. We encourage the authors to pursue their search for CD157-interacting proteins that could contribute to the pathogenesis of ovarian cancer.

CHRISTINA M. ANNUNZIATA
MICHAEL J. BIRRER

References

Notes

Affiliations of authors: Medical Oncology Branch, National Cancer Institute, Bethesda, MD (CMA); Department of Medicine, Massachusetts General Hospital Cancer Center, Boston, MA (MJB).

Correspondence to: Michael J. Birrer, MD, PhD, Department of Medicine, Massachusetts General Hospital Cancer Center, 55 Fruit St, Boston, MA 02114 (e-mail: mbirrer@partners.org).

DOI: 10.1093/jnci/djq395

© The Author 2010. Published by Oxford University Press. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

Advance Access publication on November 5, 2010.