Comment re: Preclinical Model of Spontaneous Melanoma Metastasis

In Response:

Dr. Hoffman is correct to highlight his previous work showing detection of spontaneous human melanoma brain metastases by using imaging-based techniques. Indeed, we cited one of his articles (1) mentioned in his letter as reference 16 in our Clinical Cancer Research article. We were also careful to state in our article, as noted by Dr. Hoffman, that our results represent the “first report of the detection of such spontaneous metastasis” of any human cell line, which heritably maintain this phenotype. The previous, and very elegant, studies by Dr. Hoffman and his group did indeed report detection of spontaneous brain metastases of human tumor xenografts in immunodeficient mice, but none of these metastases were harvested and then evaluated to determine if this phenotype was maintained when the cells are transplanted into new recipients. Furthermore, our report differs from previous studies in that we used as a starting point a cell line that does not metastasize to the brain (113/6-4L) to generate cell lines (131/4-5B1 and 131/4-5B2) that have specifically acquired and which retain the ability to spontaneously metastasize to central nervous system. As Dr. Hoffman notes, his prior results when combined with ours strongly support the contention that stable cell lines having a predilection for metastasis to the brain can be obtained routinely and moreover their detection should be facilitated with the use of markers such as green fluorescent protein (GFP). In this regard, we have an article in Molecular Cancer Therapeutics (2) showing emergence of brain metastases of an erbB2+/Her2+ positive variant MDA-MB-231 human breast cancer line grown in severe combined immunodeficient mice after the mice were treated with trastuzumab (Herceptin) and metronomic chemotherapy. In this model the cells we used did not have a GFP marker. However, without doubt, such an imaging marker, as noted by Dr. Hoffman, will aid future studies of the detection and response to therapy of brain metastases using brain metastatic variants.

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References

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.
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