biology and its relevance to clinical therapy. This is a laudable step along that path.

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References

Reply to the Editor:
We greatly appreciate the kind remarks and insightful comments by Konstantinov, Li, and Reddington concerning our recent manuscript, “Receptor Tyrosine Kinase and Phosphoinositide-3 Kinase Signaling in Malignant Mesothelioma.”

Although constitutive activation of the PI3K/Akt pathway has been demonstrated in a number of solid malignancies, its importance is certainly not limited to neoplastic cells. In fact, Akt signaling enhances vital cellular processes such as glycogen synthesis and nitric oxide production. LY294002 is a lead compound in the development of PI3K inhibitors and is not available for human trials. However, we believe that further drug development could possibly produce a compound with acceptable toxicity and therapeutic potential in oncology. We agree that any new interventions must be applied with caution in the context of a controlled trial.

Similarly, inhibitors of the insulin-like growth factor receptor are still in the developmental phase. While such compounds have potential as antineoplastic agents, there is also the potential for toxic effects such as the development of endocrinopathies. However, inhibitors of receptor tyrosine kinases such as epidermal growth factor receptor (Iressa, Tarceva) and platelet-derived growth factor receptor (Gleevec) are currently used in the treatment of solid and hematologic malignant tumors with acceptable side effect profiles.

We again thank Konstantinov, Li, and Reddington for their interest in our work. It is clear that an understanding of molecular mechanisms will be requisite for contemporary clinicians, particularly those treating cardiovascular and oncologic disease.

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