Vascular Smooth Muscle Proliferation as a Target for Therapeutic Intervention

To the Editor:

We read with great interest the recent article by Borel et al,1 as well as the accompanying editorial comment by Dr Bhardwaj.2 The hypothesis that vascular cell proliferation may play an important role in the pathogenesis of cerebral vasospasm has been prominently discussed for more than 15 years, and has been supported by a variety of data that have been presented over those years. We were pleased to see the addition of further support for this concept, in the form of new data showing increased levels of platelet-derived growth factor in the cerebrospinal fluid of patients with subarachnoid hemorrhage.

We would like to call attention to a misrepresentation in the article. The hypothesis that a beneficial effect of dihydropyridine calcium channel blockers in vasospasm might be attributed to block of a proliferative response and subsequent phenotypic change in vascular smooth muscle was first put forth and tested by us.3 We presented this hypothesis as an extension of previous work on the pathogenesis of atherosclerosis. In our report, which was specifically aimed at elucidating mechanisms of vasospasm, we documented the presence of L-type calcium channels in cultured smooth muscle cells and showed that proliferation (in response to serotonin) was inhibited by blocking these channels.

As noted by Dr Bhardwaj, tremendous progress has been made in advancing our understanding of cerebral vasospasm. Yet, equally tremendous gaps remain in our knowledge, including our ignorance of the molecular pathogenesis of this disorder. Only by building on prior knowledge can we hope to narrow these gaps.

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Response

We wish to thank Drs Simard and Kent for drawing to attention to their work on the effect of calcium channel blockers in preventing proliferation of cerebral smooth muscle cells.1 The work of Drs Kent and Simard indeed addressed a similar hypothesis to ours, namely, that smooth muscle proliferation contributes to the etiology of cerebral vasospasm. But although our hypotheses were similar, the modes of experimentation were quite different. Drs Kent and Simard studied the mitogenic effects of calcium channel blockers on cultured smooth muscle cells at relatively advanced passage number (passage 10 to 30). In contrast, our studies were confined to patients, whole animal models, and intact human pial arteries in vitro, and focused on the role of platelet-derived growth factors in these systems. Encouragingly, our 2 groups reached similar conclusions from our experiments: that vascular cell proliferation may indeed contribute to the genesis of vasospasm following subarachnoid hemorrhage.

In short, we agree that the conclusions published by Kent et al support the hypothesis that mitogens at the site of a clot may play an important role in the development of cerebral vasospasm. We are grateful to Drs Kent and Simard for pointing out their previous contribution in this area.

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