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.

J. Marc Simard, MD, PhD
Departments of Neurosurgery, Physiology, and Pathology
University of Maryland School of Medicine
Baltimore, Maryland

Thomas A. Kent, MD
Departments of Neurology and Pharmacology
The Program in Neurosciences
University of Texas Medical Branch
Galveston, Texas


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.

Cecil O. Borel, MD
Departments of Anesthesiology and Surgery
Duke University Medical Center
Durham, North Carolina

Laura Niklason, MD, PhD
Departments of Anesthesiology and Biomedical Engineering
Duke University Medical Center
Durham, North Carolina

Vascular Smooth Muscle Proliferation as a Target for Therapeutic Intervention
J. Marc Simard and Thomas A. Kent

Stroke. 2003;34:e108; originally published online July 17, 2003;
doi: 10.1161/01.STR.0000082484.19942.C8
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/34/8/e108

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/