Presence of Heat Shock Protein 72 in Cardiomyocytes After Heat Stress

To the Editor:

It is well-known that prior in vivo heat stress induces the synthesis of heat shock protein (HSP) 72 in the rat heart, but the precise content in the various cell-types has not yet been measured. It is therefore of great importance to conduct experiments as performed in the paper by Leger et al.1 However, the overall conclusion that heat pretreatment does not lead to HSP72 synthesis in cardiomyocytes is unjustified. In addition, the statement that blood vessels play a primary role in the heat shock–induced cardioprotection is preliminary.

The double-labeling experiments of Leger et al,1 staining HSP72, as well as HSP27, clearly indicates the presence of both proteins in the same area, which the authors define as cardiomyocytes in the case of HSP27. Indeed, other studies indicate that cardiomyocytes do overexpress HSP72 after stress: cardiomyocytes of intact hearts are capable of overexpressing HSP27 after heat treatment.2 Although the increase of HSP72 normalized for protein content was lower in cardiomyocytes than in endothelial cells, the absolute HSP72 amount was 3 times higher in the cardiomyocyte than in the endothelial cell pool. Furthermore, isolated cardiomyocytes increase their synthesis of HSP72 either after heat shock or hypoxia.3 Lastly, in cardiomyocytes, an enhanced HSP72 presence has been documented immunohistochemically after ischemia/reperfusion, after application of a nitric oxide donor, and after aortic stenosis.4,5 Because of the similar response against various stresses, it is conceivable that heat pretreatment should provoke enhanced HSP72 synthesis in cardiomyocytes. The authors should have verified the relative HSP72 amounts in cardiomyocyte and endothelial cell fractions and the endothelial specific HSP72 expression.

The authors’ statement that the beneficial effects of heat pretreatment on ischemia/reperfusion tolerance are almost exclusively due to the HSP72-induction in endothelial cells is premature. To prove this hypothesis, transgenic mice overexpressing HSP72 exclusively in endothelial cells should be generated and tested for ischemia/reperfusion tolerance. Furthermore, we do not know to what extent the increased functional recovery of the heat-pretreated hearts after ischemia/reperfusion is dependent on its absolute HSP72 content. Experiments specifically blocking the increase in HSP72-synthesis in cardiomyocytes after heat treatment would help to understand the contribution of HSP72 synthesis in these cells leading to enhanced ischemia and reperfusion tolerance.3

In our opinion, the conclusions of Leger and coworkers should be substantiated by experiments, providing exclusive evidence that heat shock–induced enhanced HSP72 expression in the endothelial cell compartment, and not in the cardiomyocyte, is responsible for the improved ischemia/reperfusion tolerance of the heart.

R.N.M. Cornelussen, PhD
F.A. van Nieuwenhoven, PhD
L.H.E.H. Snoeckx, PhD
Cardiovascular Research Institute Maastricht
Maastricht University
Maastricht, The Netherlands
A.A. Knowlton, MD
Baylor College of Medicine
Houston VA Medical Center
Houston, Texas


Response

Our study used confocal microscopy and immunofluorescence to localize heat shock protein (HSP) 27 and HSP70 in the heart after heat shock treatment.3 One of our conclusions is that after heat shock treatment, HSP70 is mainly found in blood vessels of the heart. Cornelussen and colleagues do not directly address this finding but rather interpret our findings as supporting the conclusion that heat pretreatment does not lead to HSP72 synthesis in cardiomyocytes. In relative terms, our data show that most of the increase in HSP70 is in blood vessels. Consequently, our finding of increased HSP70 in blood vessels after heat shock treatment led us to propose that blood vessels play a role in heat shock–induced cardioprotection. Our study was designed to localize anatomically HSP70 (and HSP27) in hearts, and our anatomical findings suggest a greater increase of HSP70 in blood vessels after heat shock treatment compared with cardiomyocytes, a finding that is consistent with the report of Amrani et al.2 We agree with Cornelussen and colleagues that verification, by quantitative means, of the relative amounts of HSP70 in cardiomyocytes and endothelial cell fractions after heat shock is important.

With respect to our hypothesis, given the findings of Amrani et al and our findings of HSP70 localized in blood vessels, it seems logical to propose that blood vessels play a role in myocardial protection. We agree with our colleagues that transgenic mice overexpressing HSP70 in blood vessels need to be generated and that experiments blocking HSP70 in cardiomyocytes will be essential to assess the relative contribution of increased HSP70 in blood vessels versus that in cardiomyocytes to myocardial protection, but this was beyond the scope of our study.

The letter of Cornelussen and colleagues draws attention to the importance of broadening the discussion on the contribution of each cell type in a complex organ to the phenomenon of stress-induced protection. Our work supports the notion that each cell type in an organ can have a cell-type specific response to injury. While our study shows that after heat shock treatment, HSP70 is primarily evident in cardiac blood vessels and little or no HSP70 is detected in neurons or cardiomyocytes, we agree that in response to other types of injury, such as ischemia, both neurons and cardiomyocytes express HSP70, suggesting that the cell-type specific expression of HSPs is also dependent on the kind of injury.

James P. Leger, PhD
Frank M. Smith, PhD
R. William Currie, PhD
Department of Anatomy and Neurobiology
Dalhousie University
Halifax, Nova Scotia
Canada
Presence of Heat Shock Protein 72 in Cardiomyocytes After Heat Stress
R.N.M. Cornelussen, F.A. van Nieuwenhoven, L.H.E.H. Snoeckx and A.A. Knowlton

Circulation. 2001;104:e123
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/104/22/e123

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation 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 Circulation is online at:
http://circ.ahajournals.org//subscriptions/