Atherosclerosis and Inflammatory Bowel Disease: Sharing a Common Pathogenic Pathway?

To the Editor:

The paper by Urbich et al. suggests that the CD40 pathway is involved in the vascular restenotic process. The immune-inflammatory reaction plays a critical role in atherosclerosis. In particular, the ligand for CD40 (CD40L) is involved in inflammation, thrombosis, and restenosis during progression of atherosclerosis, as discussed by Andre’ et al.2

Because of our interest in the role of the CD40/CD40L system in intestinal inflammation, we were struck by the startling similarity between atherosclerosis and inflammatory conditions of the gut, such as inflammatory bowel disease (IBD: Crohn’s disease and ulcerative colitis). First, numerous studies have found that patients with distinct cardiovascular disorders have an enhanced expression of platelet CD40L, a molecule that clusters in thrombi developing on the surface of atherosclerotic plaques.2,3 Similarly, we found that in IBD patients, platelets express CD40L in the circulation and inflamed mucosa, where microthrombosis is a prominent feature, and induce an inflammatory response in the intestinal microvasculature.4 Second, plasma soluble CD40L levels are increased in patients with cardiovascular diseases and represent a risk factor for future complications.2 We also have found that soluble CD40L plasma levels are significantly increased in IBD patients and, because of the high frequency of thromboembolic events in this population, the role of the CD40/CD40L system in IBD pathogenesis is now under active investigation. Finally, the contribution to restenosis by CD40L released by activated platelets offers a potential mechanism for the CD40/CD40L system in vessel remodeling.1

The same seems to hold true in IBD, where fibrosis is a typical complication; we have recently demonstrated the capacity of CD40L to modulate collagen synthesis and proliferation of mucosal myofibroblasts.5

In conclusion, although the ultimate molecular mechanisms underlying atherosclerosis and IBD are still uncertain and the role of the CD40/CD40L system as “primum movens” remains to be proven, sharing of this system in disease pathogenesis unexpectedly brings together 2 ostensibly unrelated conditions.

Silvio Danese, MD
Claudio Fiocchi, MD
Gastroenterology Division
University Hospitals of Cleveland
Case Western Reserve University School of Medicine
Cleveland, Ohio

Atherosclerosis and Inflammatory Bowel Disease: Sharing a Common Pathogenic Pathway?

Silvio Danese and Claudio Fiocchi

Circulation. 2003;107:e52
doi: 10.1161/01.CIR.0000055542.47474.A1

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 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/107/7/e52

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/