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.

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. 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.

Second, plasma soluble CD40L levels are increased in patients with cardiovascular diseases and represent a risk factor for future complications. 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.

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.

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.

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