Genetics of Collateral Circulation and Stroke (p 660)

Sealock et al identify a locus in the mouse genome influencing recovery from ischemic injury.

The severity of tissue damage that results from the occlusion of blood vessels is influenced by the number and size of collateral vessels in the tissue. Collateral vessels link arterioles to one another and hence can provide alternative routes for blood flow should one arteriole become blocked. Recently, a genetic locus that controls collateral size and abundance was discovered within a 27 megabase region on chromosome 7 in the mouse. Through genetic mapping techniques, Sealock and colleagues have now narrowed this region from 27 to 0.7 megabases containing just 28 protein-coding genes. Although the specific gene regulating collateral growth has not been identified, the team showed that a version of the locus associated with increased number and size of collaterals also confers improved recovery from ischemic injury.

CRP is not Proinflammatory in Healthy Subjects (p 672)

Lane et al find that C reactive protein is not proinflammatory.

Levels of C reactive protein (CRP) in the blood have long been associated with cardiovascular disease risk. And many of the known factors that cause atherosclerosis also cause levels of CRP to rise. These findings have led to speculation that CRP itself might play a causative role in atherosclerosis. Indeed, studies examining the effect of CRP on human cells in culture, on animals and even on human volunteers have indicated that CRP has a proinflammatory effect. But, Lane and colleagues say that the CRP used in most earlier studies was, a recombinant protein prepared from bacterial cultures. Thus the proinflammatory effects of recombinant CRP may have been caused by bacterial impurities. To test this idea, the team isolated and purified CRP from human plasma and infused this clinical-grade preparation at varying doses into seven healthy adults. By measuring cytokine levels and counting the numbers of neutrophils and platelets in the volunteers after CRP infusion, it was clear that none of the recipients showed any evidence of inflammation. The authors conclude that CRP itself is not proinflammatory and therefore is unlikely to be a useful target for anti-atherosclerosis treatments.

Interferon and Pulmonary Arterial Hypertension (p 677)

Interferon prompts the development of pulmonary arterial hypertension in mice, report George et al.

Pulmonary arterial hypertension (PAH), characterized by increased resistance in the lungs’ vasculature, causes strain to the right side of the heart. Left untreated the condition can ultimately lead to heart failure and death. PAH has been linked to HIV, systemic sclerosis and other conditions in which blood levels of the cytokine interferon are elevated. Furthermore, PAH is also associated with therapeutic use of interferon. Despite the accumulating circumstantial evidence, however, no causative role for interferon in PAH has been established. George and colleagues have now found more evidence of a link between interferon and PAH, showing that systemic sclerosis patients with PAH have higher levels of interferon in the blood and increased expression of an interferon receptor in the lungs of PAH patients when compared with patients without PAH. More importantly, they have also found evidence that interferon signaling is involved in the pathology of PAH. Their experiments showed that mice that lacked an interferon receptor were protected against experimentally induced PAH. These findings provide an explanation for why PAH can develop in patients receiving interferon therapy, and suggest that the interferon pathway may be a useful target for the development of new PAH treatments.
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