Reduced cardiac scarring in MMP-9–deficient mice

(See article on pages 55–62)

Healing of injured tissue typically occurs in several stages, beginning with inflammation, in which collagen and other extracellular matrix (ECM) proteins are degraded, and continuing with synthesis and deposition of new tissue and remodeling of the local ECM. Matrix metalloproteinases (MMPs) may act at each of these stages, but precise roles for individual secreted proteinases are only now emerging. Ducharme and colleagues have followed the histological changes in the left ventricle following induced myocardial infarction (MI), comparing MMP-9–deficient mice with their wild-type littermates. The earliest phases of repair occurred normally in MMP9–/– mice, but later in the process, collagen deposits were poorly organized and relatively scarce in the absence of the proteinase. Because collagen I mRNA is present at wild-type levels, the authors suggest that collagen turns over more rapidly, perhaps as a result of increased expression of several other MMPs in infarcted hearts of MMP9–/– mice. Ducharme et al. suggest that inhibition of MMP-9 might prove useful in preventing scarring after MI.

HSP70 protects the pancreas from proteolytic injury

(See article on pages 81–89)

The exocrine pancreas is the source of trypsinogen and other latent digestive enzymes that can be activated once trypsinogen is cleaved to generate trypsin. The cells of the pancreas are normally protected from injury by maintaining this proenzyme in its uncleaved form. Working with rat pancreas fragments in organ culture, Bhagat et al. show that treatment with the secretagogue cerulein, which can cause pancreatitis in vivo, induces trypsinogen activation and cell damage. They also show that the stress response protein HSP70, a normal cell component that accumulates to high levels during the culture of pancreas fragments, helps protect these cells from secretagogue-induced injury. Antisense oligonucleotides targeted to HSP70 block this protective effect and allow trypsinogen to become colocalized with lysosomal hydrolases, which presumably mediate its activation. The flavonoid drug quercetin specifically inhibits transcriptional induction of HSP70, and it also induces activation of trypsinogen. How HSP70 might influence trypsinogen localization within the cell is not known.