Pim-1 and Chromatid Segregation  
Sundararaman et al report that asymmetry is best when it comes to progenitor cell chromatid division, and Pim-1 can help.

Stem cells do not divide up their chromatids randomly at cell division. After DNA replication, sister chromatids are selectively distributed to daughter cells, though whether this is due to one cell always retaining the template strands—the immortal strand hypothesis—or is dependent on epigenetic differences between chromatids—the silent sister hypothesis—is not clear. Whatever the precise mechanism, this asymmetric chromatid division is thought to be essential for stem cell self-renewal. That is, the ability of cardiac progenitor cells (CPCs) to self-renew might improve their long-term effectiveness in repairing injured myocardium. Previous research from this laboratory had shown that the kinase, Pim-1, could increase proliferation of CPCs. And now, the authors show that Pim-1 also drives a 2-fold increase in CPC asymmetric chromatid segregation. Overall, the results suggest that Pim-1 kinase might be an important tool for maximizing the effectiveness of CPC-based cardiac repair strategies.

Platelets in Encephalomyelitis  
Platelet perpetrators exacerbate multiple sclerosis pathology, report Langer et al.

Multiple sclerosis (MS) is a disease in which the body’s own immune cells attack the myelin sheaths that surround and protect neurons in the central nervous system. As a consequence, neuronal function is impaired causing an array of debilitating physical and cognitive disabilities. A recent expression profiling study of postmortem MS patient brain lesions revealed an upregulation of a platelet adhesion receptor transcript. This led Langer et al to investigate whether platelets might play a role in MS disease pathology. They found that platelets were indeed abundant in the brain lesions of MS patients and of mice with experimental autoimmune encephalomyelitis (EAE)—an animal model of MS. They also showed that depleting platelets in EAE mice reduced the recruitment of other inflammatory cell types to the inflamed CNS. And, importantly, that it considerably improved the disease symptoms in the mice. Blocking the adhesion receptors on the platelet cells with antibodies produced similar results. Together the data show that platelets are important perpetrators of MS pathology and that targeting these cells might be a novel therapeutic approach to consider.

Nox4 and NADPH Oxidase  
Nox4, unlike close relatives Nox1 and 2, is a vascular do-gooder, say Schröder et al.

The Nox family of enzymes produces reactive oxygen species (ROS), such as superoxide (O$_2^-$) and hydrogen peroxide (H$_2$O$_2$). ROS are generally considered detrimental to cells and Nox1 and 2 have been pinpointed as mediators of endothelial dysfunction. Overexpressing Nox4, however, exerts beneficial vascular effects, such as improved endothelial function and angiogenesis. Schröder et al show that Nox4 does indeed promote vascular protection. They studied mice lacking Nox4 and found that although these mice produced less H$_2$O$_2$ in their vascular endothelial cells, they also produced less nitric oxide synthase—an enzyme that makes the crucial vasodilator, nitric oxide. The mice were also worse at recovering from muscle ischemia: capillary density and blood flow in their recovering muscles was lower. It turns out that a small amount of H$_2$O$_2$ is a good thing. Nox4 primarily produces H$_2$O$_2$, whereas Nox1 and 2 tend to produce more O$_2^-$, which interacts with and dampens the effect of nitric oxide. Nox4 inhibitors are currently being developed for use in stroke where the enzyme is thought to cause neuronal damage. So, the authors warn, such drugs should be monitored for vascular side effects.

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