Stroke Activates the Bone Marrow (p 407)

Courties et al identify the source of inflammatory immune cells after a stroke. Stroke is caused by an interruption of blood flow to the brain due to hemorrhage or occlusion of a blood vessel. The resulting ischemic injury triggers the recruitment of inflammatory immune cells, which are essential for clearing the damaged tissue, but can cause further damage if the response is excessive or prolonged. To determine whether immune cells were recruited to the brain from elsewhere in the body after a stroke, or were made afresh in the bone marrow, Courties and colleagues studied the bone marrow cell activity in mice after experimentally induced stroke. They found that rates of cell division—specifically of hematopoietic stem cells (HSC)—were increased. As a result, the numbers of both neutrophils and monocytes were increased as well. There was also an increase in the bone marrow levels of noradrenaline, and the team found that this hormone drove the HSC proliferation: mice that lacked the β3 adrenergic receptor for noradrenaline failed to exhibit increased HSC proliferation after stroke. Knowing the source of the immune cells may offer new ways to reduce their recruitment to the brain and thus diminish tissue damage after a stroke. But given the essential role of the immune response in tissue repair, further studies will be necessary to determine how to fine tune the response to maximize brain recovery.

MicroRNA Induced Cardiac Reprogramming In Vivo (p 418)

In vivo cardiac reprogramming with microRNAs improves heart function, report Jayawardena et al. The scar tissue formed after a myocardial infarction reduces the contractility and function of the heart; leading often to heart failure. To simultaneously reduce scar tissue and increase heart function researchers are investigating ways to reprogram the scar fibroblasts directly into cardiomyocytes. Such reprogramming has been shown to work in mice using different combinations of either transcription factors or microRNAs (miRs). But while reprogramming with transcription factors has been shown to result in functional improvements in the heart muscle, whether the same is true for miR-based reprogramming is not known. Moreover, it is unclear whether miR reprogramming leads to the formation of fully differentiated cardiac myocytes. Jayawardena and colleagues therefore examined miR-based reprogramming more closely. They found that around the injury zone of infarcted mouse hearts injection with miRs led to a three-fold increase in cells expressing a marker of mature cardiac myocytes. Furthermore, these reprogrammed cells closely resembled mature ventricular cardiac myocytes in their electrophysiological behavior. But importantly, the team showed that miR reprogramming of injured hearts improved heart function in mice. Although reprogramming with either method—transcription factors or miRs—remains inefficient, these new results validate the miR-mediated reprogramming as a viable method worthy of further optimization.

TMAO Promotes Renal Fibrosis and Dysfunction (p 448)

A choline-rich diet may contribute to chronic kidney disease, say Tang et al. During the breakdown of dietary choline, microbes residing in the gut generate the metabolite trimethylamine N-oxide (TMAO). High levels of TMAO in the blood have been associated with both chronic kidney disease (CKD) and coronary artery disease, but it is not clear whether TMAO can directly contribute to these conditions. Hence, Tang and colleagues examined the link between TMAO and CKD in a large cohort of subjects and discovered that individuals with CKD had markedly higher TMAO levels than those without CKD. Furthermore, within the group of CKD patients, those with the highest levels of TMAO were at a greater risk of dying. To determine whether TMAO could directly lead to CKD, the team fed mice a diet rich in either TMAO, or choline. They found that when placed for six weeks on either diet, the mice displayed increased blood levels of TMAO. The mice also exhibited signs of renal injury, characterized by increased amounts of the kidney injury marker 1 (KIM1), fibrosis of the kidney tubule interstitium, and impaired renal function. Together the results suggest not only that TMAO is a useful prognostic marker of CKD, but that diets low in choline—which is found in red meat, egg yolks, liver, and high-fat dairy products—may help in preventing, or slowing the progression of, CKD.