Whether heart cells grow wide or long depends on ERK1/2 signaling, say Kehat et al. Many studies implicate ERK1/2 signals in cardiac hypertrophy, but mouse models designed to overexpress or lack ERK1/2 have provided seemingly contradictory results. Overexpression leads to a type of hypertrophy called concentric hypertrophy, in which the heart cells thicken, but genetic deletion of ERK1/2 does not stop the heart from enlarging. Kehat et al now resolve the issue by showing that ERK1/2 controls the way heart cells grow. Without ERK1/2, heart cells lengthened rather than thickened. Such growth was apparent in the hearts of the transgenic mouse models, as well as from heart cells in culture in which ERK1/2 expression was acutely controlled. This suggests ERK1/2’s effects are direct rather than secondary, say the authors. Pressure overload in the heart tends to make heart cells thicken, whereas volume overload tends to lengthen them. Confusingly, both types of hypertrophic stimuli activate ERK1/2. One possible explanation is that although ERK1/2 simply promotes cell thickening, it loses the battle to length-promoting signals in situations of volume overload. Because pathologic hypertrophy can lead to heart failure and death, discovering ERK1/2’s downstream targets and precisely how it controls the hypertrophic response could ultimately save lives.

Pagler et al show how good cholesterol (HDL) promotes macrophage migration away from atherosclerotic plaques.

Atherosclerotic plaques are formed in part by the accumulation of foam cells—macrophages and smooth muscle cells carrying excessive amounts of bad cholesterol (LDL). HDL helps clear LDL from foam cells by the action of the fat-transporting proteins, ABCA1 and ABCG1. HDL thus helps to prevent the formation of atherosclerotic plaques or to remove plaques that have started to form. Plaque reduction, or regression, is associated with migration of macrophages away from the plaque toward local and systemic lymph nodes. Pagler et al wondered whether HDL and ABCA1/G1 were also controlling this migration. In vitro migration assays showed that wild-type macrophages moved in response to HDL, but ABCA1/G1-lacking macrophages did not budge. The team further showed that in the ABCA1/G1-lacking cells, sterols accumulated at the cytosolic face of the plasma membrane and, in turn, activated Rac1, a signaling molecule that controls many cellular functions including cytoskeletal reorganization and cell motility. Boosting HDL has been suggested as a therapeutic intervention to stop and reverse atherosclerosis. Pagler et al show, at least in part, how such therapy would work.

Size might not be everything when it comes to calcium-release events, report Brochet et al. In a heart cell, calcium release from the sarcoplasmic reticulum (SR) occurs in discrete events called sparks. Calcium is released from the SR via membrane channels called ryanodine receptors, which are organized into clusters called calcium release units (CRUs). It was thought that under normal physiologic conditions, sparks were the only mode of calcium release event, but recent evidence suggests that smaller events dubbed “quarks” might also exist. Because such low-level release events are hard to resolve from the noise, Brochet et al took a novel approach of simultaneously measuring drops in calcium level inside the SR (blinks), as well as their corresponding cytosolic sparks. This enabled the detection of “true” release events and, importantly, confirmed the existence of quarks. Although the amount of calcium released by quarks as tiny compared with sparks, quarks were much more frequent, thus overall their contribution to calcium release was similar. The authors suggest that quarks might arise from rogue ryanodine receptors, those spatially separated from CRUs. Whatever their source, because faulty calcium-release events underlie potentially fatal arrhythmias, understanding the mechanisms and the effects of quarks will be important for the future of arrhythmia research and treatment.
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