Cardiac Cellular Diversity (p 400)

Pinto et al catalogue the cellular composition of mouse and human heart tissues.

Knowing the identity and the abundance of different cell types within the mammalian heart is essential for understanding myocardial development, disease pathologies, and cardiac regeneration. Although cardiomyocytes make up the majority of the mass of the heart, in terms of actual cell numbers. These cells are not the most abundant. Furthermore, despite previous research, it remains unclear whether fibroblasts or endothelial cells are the most numerous cells in the heart. To resolve this issue, Pinto and colleagues performed immunohistochemical and flow cytometric analyses on cells isolated from mouse and human hearts. They found that in both mice and humans, cardiomyocytes comprised approximately 31 percent of the total cell number, while of the nonmyocyte cells, the endothelial cells were by far the majority—about 60 percent. Fibroblasts, on the other hand, constituted less than 20 percent. In addition, between 5% and 10% of cells in the heart were of hematopoietic origin. The finding that endothelial cells are the most abundant cells in the heart suggests that these cells play a greater role in heart physiology, pathology, and response to injury than had been assumed previously.

USP2 Counteracts IDOL-Mediated LDLR Degradation (p 410)

USP2 increases cellular uptake of “bad” cholesterol by preventing degradation of the LDL receptor, report Nelson et al.

The LDL receptor (LDLR) is the major pathway for the clearance of LDL from the blood into the liver. Indeed, mutations in the LDLR gene lead to hypercholesterolemia, accelerated atherosclerosis and premature mortality. Once internalized the LDLR is tagged with ubiquitin, by a protein called inducible degrader of LDLR (IDOL), which marks the protein for destruction. Because IDOL activity reduces LDL uptake, suppression of IDOL function might be an effective approach to improve LDL clearance in patients with high cholesterol. Therefore, Nelson and colleagues searched for intracellular binding partners of IDOL. They found that a protein called USP2, an enzyme that removes ubiquitin tags, strongly stabilized the IDOL protein. Instead of increasing IDOL-dependent degradation of LDLR, however, USP2 activity paradoxically decreased LDLR degradation. Using co-immunoprecipitation experiments, the team found evidence consistent with the notion that LDLR, IDOL and USP2 form a tripartite complex at the plasma membrane. Based on these observations, the authors suggest that even though USP2 stabilizes IDOL it might also stabilize LDLR. Regardless of the mechanism, their results indicate that USP2 is an important inhibitor of LDLR degradation and as such could be a potential target for future LDL-lowering therapies.

Plasma MicroRNAs and Platelet Function (p 420)

Kaudewitz et al examine the relationship between platelets and small plasma RNAs.

Although microRNAs (miRs) regulate the expression of target mRNAs within cells, they can also be secreted and are found circulating in the blood. Particular signatures of miRs in the plasma have been associated with cardiovascular events and disease risks. Furthermore, in patients with atherosclerosis, treatment with platelet inhibitor drugs reduces plasma levels of platelet-related miRs. Kaudewitz and colleagues now extend these observations, showing that in patients receiving platelet-inhibitors and health volunteers, platelet activity is positively associated with plasma levels of both miRs and YRNAs—another type of small noncoding RNA with largely unknown function. By extracting platelets from the volunteers’ blood, concentrating and reinjecting the cells, the team showed that plasma levels of both types of small RNAs increased, confirming that these RNAs were indeed derived from platelets. The team also found that suppressing the activity of platelet-derived miR-126 in mice could reduce platelet aggregation. In humans, a genetic variant of miR-126, which boosts levels of this miR, is similarly associated with platelet activation. Together these results suggest that miRs may not only reflect, but also influence platelet activity.