In heart failure, Kumarswamy et al. discover an RNA biomarker for heart failure.

Patients that survive a heart attack often develop cardiac remodeling and heart failure, but there are few indicators that help to determine which patients are most at risk. In cancer research, extracellular RNAs have been identified in blood plasma as potential biomarkers of disease. Whether heart failure patients might also have clinically informative plasma RNA profiles, however, has not been investigated. Thus, Kumarswamy and colleagues decided to analyze long non-coding RNAs in the plasma of patients who had suffered myocardial infarctions. Using ECG data, the team compared 15 patients who exhibited the most extreme heart remodeling with 15 who exhibited no remodeling at all. They found seven candidate RNAs that differed between these two extreme remodeling groups, but after examining the candidates in an additional 216 patients, only two consistently correlated with heart remodeling. They picked one, called it LIPCAR (Long Intergenic non-coding RNA Predicting Cardiac Remodeling) and went on to examine its levels in patients with chronic heart failure. Not only was the level of LIPCAR even higher in these patients, but it was able to reliably predict those patients most at risk of suffering fatal cardiovascular events. Although it is not clear exactly why LIPCAR levels increase as heart failure worsens, the RNA still has the potential to be a valuable marker for both tracking and predicting disease progression.

The receptor TLR4 on platelets drives the development of pulmonary hypertension, according to a report by Bauer et al.

Pulmonary hypertension—increased blood pressure in the lung vasculature—is a severe and often fatal disease. It was traditionally thought to be triggered by vasconstriction; however, it is now known that other mechanisms, including thrombosis and inflammation, can also contribute to and even initiate the disease. Indeed, recent evidence suggests that the innate immune receptor TLR4 is involved in the pathology of pulmonary hypertension, although its exact role remains unclear. Bauer and colleagues have now shown that mice lacking the receptor were more resistant to experimentally induced pulmonary hypertension. They also discovered that specific deletion of the receptor from platelets conferred this resistance, but that its deletion from myeloid cells had no effect. Unlike their wild-type counterparts, TLR4-lacking platelets failed to activate the development of pulmonary hypertension. This prevented the characteristic vascular remodeling—such as vessel wall thickening and increased vessel muscularization—associated with the disease. Taken together, the results suggest that blocking interactions between TLR4 and its endogenous ligands could be an effective strategy for treating pulmonary hypertension.

Hilgendorf et al. investigate the macrophage and monocyte milieu after myocardial infarction.

After a heart attack, the removal of damaged tissues and debris is important, but so too is minimizing the scar tissue, which can diminish the functionality of the myocardium. Therefore, an initial inflammatory phase involving recruitment of monocytes expressing high levels of the surface glycoprotein Ly-6C gives way to a reparative phase directed by cells expressing low levels of Ly-6C. It is unclear whether this transition from high to low Ly-6C expression is due to the recruitment of new cells or to the differentiation of high Ly-6C expressing monocytes into low-expressing macrophages. Hilgendorf et al. now report that the latter is, in fact, responsible. They found that mice lacking the transcription factor Nr4a1—which is essential for producing low Ly-6C-expressing monocytes, but not macrophages—could still accumulate low Ly-6C-expressing macrophages in the heart after infarction. Since these mice do not produce low-expressing monocytes at all, the low-expressing macrophages must have been derived from high-expressing monocytes. The team also showed that, coincident with transition to the repair phase, Nr4a1 levels increased in the heart, which reduced the recruitment of high Ly-6C-expressing inflammatory monocytes. Thus, because Nr4a1 controls the transition from inflammation to repair, the transcription factor could prove a valuable target of future treatment strategies aimed at minimizing the development of scar tissue in heart failure.
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