IN THIS ISSUE

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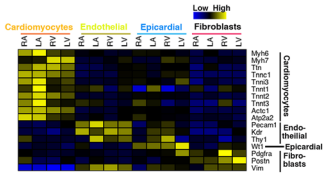
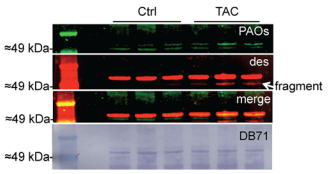


Airn in Cardiomyocytes (p 1347)

Hosen et al discover a novel role for the imprinting RNA *Airn* in heart cells.

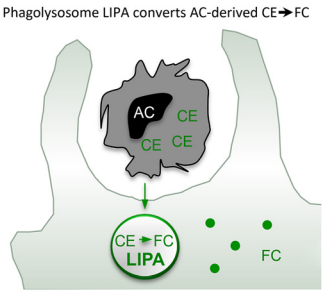
Airn is a long noncoding RNA that is antisense to and that silences the *Igf2r* (insulin-like growth factor 2 receptor) gene via developmental imprinting (expression of *Airn* from the paternal chromosome shuts down *Igf2r* expression from the maternal chromosome). But aside from its role in imprinting, *Airn* is sometimes capped, polyadenylated, and spliced just like a regular mRNA (messenger RNA). However, it is not known whether these spliced isoforms of *Airn* have functional roles, and what those functions might be. Hosen and colleagues have now investigated the role of one of these spliced forms, called *Airn-001*, in the heart. The team initially discovered that both *Airn* and *Airn-001* were downregulated in the hearts of mice following infarction. They then showed that in mouse cardiomyocytes *Airn-001* was preferentially expressed in the nucleus, just like unspliced *Airn*, but was also more stable. Both *Airn* and *Airn-001* were shown to associate with an mRNA-binding protein called Igf2bp2, and this interaction boosted translation of certain mRNAs normally targeted by the protein. Together, these results identify a novel role of *Airn* RNAs in translation regulation that could be relevant to the physiology of cardiac myocytes in both normal and postinfarction hearts.



Desmin Forms Preamyloid Oligomers in Heart Failure (p e75)

Monophosphorylated desmin forms protein clumps during heart failure, report *Rainer* et al.

Toxic aggregates of proteins accumulate in the brain in several degenerative diseases, such as Alzheimer and Parkinson disease. But such aggregates, or amyloids, have also been observed in heart failure. Indeed, in both dogs and humans, an aggregation-prone form of the cytoskeletal protein desmin accumulates in the failing myocardium. Rainer and colleagues now show that this aggregation-prone desmin accumulates in the hearts of mice with induced heart failure as well. Moreover, they show that the modified desmin (the protein is monophosphorylated at serine 31) actually promotes the formation of protein aggregates in rat ventricular cardiomyocytes. In contrast, biphosphorylated desmin—considered to be the physiological form of the protein—did not prompt the formation of such aggregates. The team went on to show that positron emission tomography could detect the aggregates in live mice and that the small molecule epigallocatechin gallate could disrupt the aggregates in vitro. The work, thus, not only identifies the post-translationally modified form of desmin responsible for the formation of toxic aggregates, but also identifies tools for manipulating and detecting these aggregates in future research.



LIPA and Efferocytic Inflammation (p 1369)

Impaired lysosomal activity in macrophages leads to chronic inflammation in atherosclerosis, say *Viaud* et al.

By removing modified lipoproteins and clearing dead and dying cells (efferocytosis), macrophages play an essential role in both cholesterol homeostasis and preventing inflammation. Macrophages process the phagocytosed material in lysosomes. Indeed, mice and humans deficient in lysosomal acid lipase (LIPA) activity exhibit dyslipidemia, accelerated atherosclerosis, foam-cell formation, and tissue inflammation. Nevertheless, it remains unclear how LIPA deficiency leads to macrophage dysfunction. Viaud and colleagues investigated the role of LIPA in human macrophages in a series of experiments involving either overexpression or inhibition of LIPA. They found that inhibition of LIPA hinders macrophage efferocytosis—via defective phagocytic cup formation—and activates the expression of inflammasome factors. In experiments with mice with hypercholesterolemia, the team found that LIPA inhibition prompts defective clearance of stressed erythrocytes and apoptotic lymphocytes, leading to an increase in inflammation. Together, these findings support recent genome-wide association studies implicating LIPA as a cardiovascular disease susceptibility gene.

Written by Ruth Williams
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