IN THIS ISSUE

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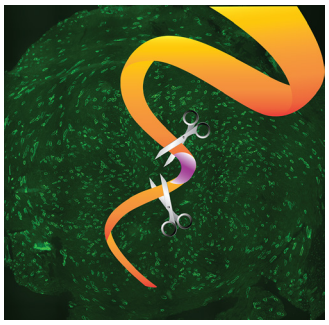
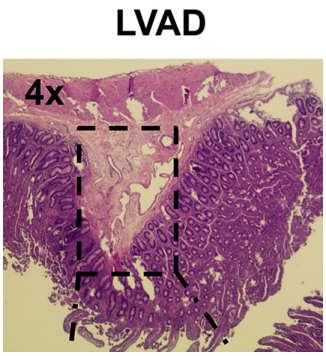


Genome Editing Therapy for DMD Cardiomyopathy (p 923)

Editing the dystrophin gene improves heart muscle function in mice with muscular dystrophy, report *El Refaey* et al.

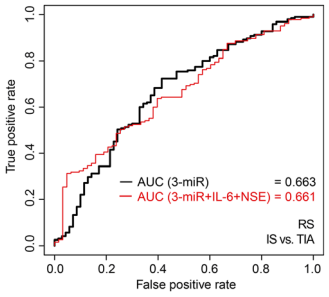
Duchenne muscular dystrophy (DMD), the most common form of muscular dystrophy, is caused by mutations to dystrophin—a protein essential for the structural stability of muscle cells. There is no cure for DMD and patients face a life of slowly degenerating muscles, and death normally occurs in early adulthood—most often because of weakened heart and lung muscles. But now, because of CRISPR gene editing technology, there is hope for a new treatment with permanent effects. Indeed, mice with muscular dystrophy have had their dystrophin levels partially restored and skeletal muscle function improved as a result of dystrophin gene editing. In these studies, however, functional improvements to the heart were not explored. El Refaey and colleagues now show that a single dose of dystrophin-targeted gene-editing vectors can improve heart muscle function in mice. Following intravenous injections of the vectors into pups with severe muscular dystrophy, nearly half of the animals' cardiac myocytes became positive for dystrophin, while their hearts displayed reduced fibrosis, and their isolated cardiac muscles had improved contractility. Overall, these results support the idea that gene editing has the potential to become a valuable future treatment for DMD.



LVADs Cause Angiodysplasia (p 963)

Kang et al identify a likely reason for intestinal angiodysplasia in left ventricular assist device users.

Left ventricular assist devices (LVADs) are surgically implanted mechanical pumps that temporarily or permanently help patients with weakened hearts to maintain sufficient blood circulation. But, for reasons that are largely unclear, between 18% and 40% of LVAD patients start bleeding from their gastrointestinal tracts. It is known that use of LVADs is associated with degradation of von Willebrand factor (vWF), deficiency of which causes increased bleeding and vascular malformations. Thus, Kang and colleagues hypothesized that disrupted vWF function in LVAD patients may be the cause of gastrointestinal bleeding. The team examined the intestines of deceased individuals with and without LVADs, as well as euthanized cows and sheep with and without the devices. They found that LVAD use was linked with increased vascularity of the gut and that these vessels were abnormally structured and organized. Furthermore, blood samples from 41 LVAD-supported patients revealed evidence of vWF degradation. While the mechanistic process linking LVAD use with vWF degradation remains unclear, the work suggests that preventing such degradation might be a worthy target for avoiding angiodysplasia in LVAD patients.



miRNAs as Biomarkers After Stroke (p 970)

Tiedt et al identify 3 microRNAs as potential biomarkers of acute ischemic stroke.

Stroke is the second most common cause of death and primary cause of long-term disability world wide. While most strokes are due to brain ischemia, others are caused by hemorrhage, and determining which form a patient has is critical for subsequent treatment. CT scans of acute stroke victims help identify the cause, but ≈40% to 50% of ischemic stroke sufferers lack detectable abnormalities. Blood-based biomarkers would, therefore, be a helpful addition to the diagnostic toolbox. Tiedt and colleagues reasoned that microRNAs (miRs), because of their stability in peripheral blood, might be informative biomarkers. Thus, they sought to identify differentially regulated miRs between patients with ischemic stroke and controls. RNA sequencing of blood samples taken from 260 acute ischemic stroke patients on the day of hospitalization revealed 3 miRs that were robustly and reproducibly upregulated in patients: miR-145-3p, miR-125b-5p, and miR-125a-5p. The team went on to show that levels of all 3 miRs declined in the days following acute stroke. In combination, these miRs outperformed CT scans for diagnostic utility. These encouraging findings now pave the way for further studies in larger cohorts of acute ischemic stroke patients.

Written by Ruth Williams
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