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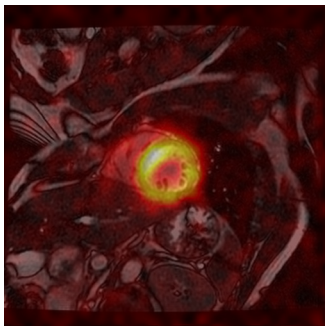
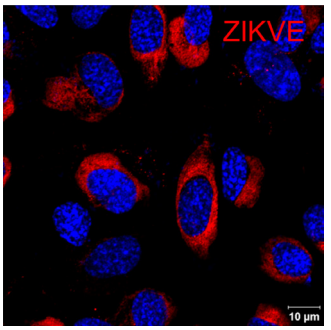


Hyperpolarized MRI of the Human Heart (p 1177)

***Cunningham* et al perform hyperpolarized ^{13}C MRI in healthy humans to observe metabolism in the heart.**

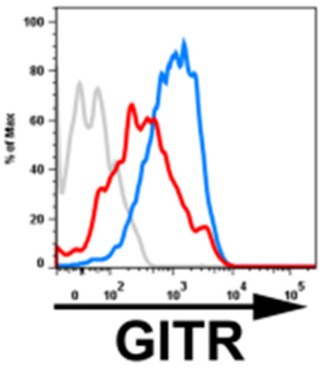
Heart failure is accompanied by changes in cardiac metabolism. However, assessing myocardial metabolism in heart failure patients is technically challenging and limited by a lack of appropriate methodologies. For example, magnetic resonance spectroscopy (MRS), which is used currently to assess metabolic changes, has poor sensitivity and detects only a limited range of biochemical reactions. Similarly, positron emission tomography (PET) can be used to measure metabolic activity, but provides no information about individual metabolic reactions. PET also delivers a high dose of radiation and, therefore, cannot be used very frequently. A newly developed technique called hyperpolarized ^{13}C MRI offers enhanced imaging of carbon-containing substrates and their metabolites. Indeed, hyperpolarized pyruvate is currently being tested in clinical trials for visualizing altered metabolism in tumors. Now, Cunningham and colleagues have tested hyperpolarized pyruvate in 4 healthy individuals to examine metabolism in the heart. Immediately after hyperpolarized pyruvate injection, the subjects were scanned, and levels of pyruvate, bicarbonate, and lactate were measured. Pyruvate was detected mainly in the chambers of the heart, bicarbonate in the myocardium, and lactate in both. Importantly, all subjects tolerated the procedure, and no adverse events occurred. This work provides the first images of the human heart obtained with hyperpolarized ^{13}C MRI and suggests that the technique may be more useful than current approaches for assessing cardiac metabolism in heart failure patients.



Zika Virus Infects Endothelium (p 1183)

Endothelial cells are targets for zika virus, report *Liu* et al.

Generally transmitted by mosquitoes, the zika virus is a blood-borne pathogen, but it has also been detected in other tissues, including saliva, semen, urine, fetal tissues, and the central nervous system. Indeed, zika has been confirmed as the cause of microcephaly in babies born to infected mothers. The blood–brain barrier (BBB) and placental–blood barrier (PBB) are specialized regions of the endothelial lining of blood vessels that help prevent viruses and other factors in the blood from entering the brain and fetal tissues. Zika, however, appears to be able to transgress both the BBB and PBB. Liu and colleagues, therefore, examined whether zika was capable of infecting endothelial cells. They cultured immortalized human BBB endothelial cells and found that 4 different strains of zika could readily infect them, and even produce progeny. A dengue virus strain, used as a control, could not. The team went on to show that primary endothelial cells from a variety of sources were also susceptible to zika infection, and that a cell-surface receptor called AXL—previously implicated in zika infectivity—was required for virus entry. The finding that zika readily infects endothelial cells could explain how the virus propagates through a variety of tissues and suggests that endothelial cells and AXL could be possible targets for antiviral therapies.



Treg Plasticity in Atherosclerosis (p 1190)

Atherosclerosis promotes the production of ineffective Tregs that exacerbate the disease, say *Butcher* et al.

T-regulatory cells (Tregs) are immunosuppressive cells that balance the need to fight infections with the need to limit tissue damage and resolve inflammation. However, Treg numbers decline in atherosclerosis, and Treg depletion most likely contributes to the chronic inflammation associated with the atherosclerotic disease. To examine the fate of Tregs in atherogenesis, Butcher and colleagues examined Treg populations in atherosclerosis-prone mice. They found that a significant proportion of the animals' Tregs had in fact adopted a change of phenotype, whereby they exhibited a more Th1-like (proinflammatory) state. The cells continued to express Treg markers, such as the transcription factor Foxp3, but their expression of immunosuppressive genes was reduced and that of proinflammatory genes increased. These hybrid Th1-like Treg cells failed to suppress both T-cell responses in vitro and arterial inflammation in atherosclerosis-prone mice. Control Tregs, on the other hand, attenuated atherosclerotic lesion formation. These results indicate that dysfunctional Th1-like Tregs essentially permit atherogenesis by failing to suppress inflammation, and suggest that therapeutically bolstering Tregs against a Th1-like fate might be an effective strategy for slowing atherogenesis.

Written by Ruth Williams

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