Lipoprotein Apheresis Removes Plasma PCSK9 (p 1290)

Removing low-density lipoprotein (LDL) from the blood of patients decreases PCSK9—an LDL regulator, report Tavori et al.

Lipoprotein apheresis is a blood cleaning treatment in which the blood of patients with hypercholesterolemia is purged of the LDL-containing fraction. It is a highly effective method of removing LDL—often resulting in a decrease of up to 80%. Now Tavori et al report that an added benefit of this process (apheresis) is the removal of a protein called PCSK9. PCSK9 binds and suppresses the LDL-receptor, ultimately hindering the removal of LDL from blood. But recent work revealed that PCSK9 does not just bind the LDL receptor. It also binds LDL itself. Building on these observations, Tavori and colleagues hypothesized that along with LDL, lipoprotein apheresis might also remove PCSK9 from the blood—and indeed it did. In fact, apheresis removed much more PCSK9 than expected and much of it was LDL-free. The authors suggest that the removal of PCSK9 during apheresis could contribute to the maintenance of low levels of LDL between treatment sessions. Importantly, these findings lend further support to the development of PCSK9-inhibition strategies for use either alone, or in conjunction with apheresis.

Beta1 Integrin, a Direct Target of miR-223 (p 1320)

Exercise improves HDL function in patients with chronic heart failure, report Adams et al.

Although elevated blood levels of high-density lipoproteins (HDL) are associated with a decreased risk for heart disease, simply raising HDL in patients that have suffered acute cardiovascular events does not reduce the risk of a recurrence. Indeed, evidence suggests that HDL function is also impaired in patients with cardiovascular disease. Adams and colleagues thus compared the function of HDL isolated from healthy people with that from patients with chronic heart failure. While HDL is known to protect the vascular endothelium in a number of ways—by promoting reverse cholesterol transport, diminishing inflammation, and stimulating vasodilation via nitric oxide (NO) production, the team focused on this latter effect only. They found that, compared with HDL from healthy subjects, HDL from patients with heart failure had a reduced capacity to stimulate NO production in cultured human endothelial cells. They then tested HDL isolated from subjects that had undergone 12 weeks of aerobic training. Their results showed that exercise training enhanced the NO producing capacity of HDL in heart failure patients, although in healthy subjects, exercise training had no effect on HDL. These findings suggest that heart failure impairs HDL function and that improving HDL function may be one of the reasons why exercise training benefits these patients.

MicroRNA-223 prevents proliferation of endothelial cells and is antiangiogenic, say Shi et al.

Adult vascular endothelial cells are normally quiescent; however, after injury they proliferate, migrate, and contribute to the repair of existing vessels and/or the growth of new vessels. The growth factor VEGF, a major regulator of blood vessel growth, has been shown to activate several microRNAs (miRs)—small noncoding regulatory RNAs—in cultured endothelial cells. But Shi and colleagues were interested in finding such angiogenesis-related miRs expressed in native endothelium. The team therefore compared the miRs expressed in freshly isolated cells with those expressed in proliferating, cultured endothelial cells. They found that one specific microRNA, miR-223, was highly expressed in the freshly isolated cells, but was dramatically down-regulated once the cells were cultured. They also found that miR-223 was further suppressed by VEGF treatment, and overexpressing miR-223 attenuated VEGF-induced proliferation of endothelial cells. Furthermore, in vivo suppression of miR-223 boosted neovascularization after ischemia. The team went on to show that miR-223 exerts its antiangiogenic effects by directly suppressing the expression of β1 integrin—a known proangiogenesis factor. Thus it seems that miR-223 could be a new regulator of blood vessel growth and repair.

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