

Exercise Corner

Another Molecule Generated by Exercise Protects the Brain *Anthony L. Komaroff, MD*, reviewing De Miguel Z et al. Nature 2021 Dec Clusterin prevents activation of inflammation-related genes in brain endothelial cells. Epidemiologic studies show that regular exercise is associated with improved cognition. Recently, a molecule generated by exercise, irisin, was shown to protect the brain, in part by limiting neuroinflammation (*NEJM JW Gen Med Oct 15 2021* and Nat Metab 2021; 3:1058). In a new study, researchers identified another molecule that also prevents neuroinflammation and protects cognition. Plasma harvested from regularly exercising mice was infused into young mice that were not able to exercise regularly. This infusion activated specific genes that inhibited neuroinflammation, especially genes that inhibited the complement cascade - and particularly the gene for a molecule called clusterin. Clusterin bonded to endothelial cells in the brain and prevented activation of inflammation-related genes in the endothelial cells.

Treatment with clusterin reduced experimentally induced neuroinflammation in both normal mouse strains and in a mouse model of Alzheimer disease. None of these beneficial changes were seen in control mice infused with saline, nor in mice infused with plasma from exercising mice in which clusterin had been depleted by antibodies. Twenty men with amnestic mild cognitive impairment then were started on a program of regular physical exercise for 6 months. Before-and-after studies showed a marked rise in their levels of clusterin, showing that the mouse studies might be applicable to humans. COMMENT The mechanisms by which regular exercise protects the brain are being revealed gradually. Perhaps this knowledge someday will be used to confer the cognitive benefits of exercise through novel pharmacotherapy

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