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Putting the brakes on sepsis

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Sepsis—an extreme response to infection—can cause damage to multiple organ systems when it triggers an uncontrolled inflammatory response.

C. Henrique Serezani, Ph.D., and colleagues are seeking molecular "brakes" that will dampen sepsis-induced inflammation and prevent organ damage. They investigated a role for an enzyme called PTEN, a lipid and protein phosphatase that regulates various pathways of the immune response.

They found increased expression of the PTEN gene in white blood cells from patients and mice with sepsis, but greatly reduced levels of PTEN protein in septic patients with severe illness. The researchers showed that blocking PTEN genetically or pharmacologically increased bacterial load, inflammation, lung injury and death in mice with sepsis. They demonstrated that PTEN induces the production of microRNAs that regulate gene expression to reduce inflammatory signaling.

The findings, reported May 1 in *Science Signaling*, identify a previously uncharacterized role for PTEN in regulating microRNA production and decreasing the mortality and comorbidities associated with sepsis.

More information: Nuclear PTEN enhances the maturation of a microRNA regulon to limit MyD88-dependent susceptibility to sepsis. *Sci. Signal.* 01 May 2018: DOI: 10.1126/scisignal.aai9085