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A boost in microRNA may protect against sepsis and other inflammatory diseases

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Acute inflammatory diseases, such as sepsis, as well as chronic inflammatory diseases like diabetes and arthritis, develop as a result of sustained inflammation of the blood vessel wall. Researchers at Brigham and Women's Hospital (BWH) have discovered that a microRNA (small, non-coding RNA molecule) called miR-181b can reduce the inflammatory response that is responsible for such diseases.

The findings, by researchers led by Mark Feinberg, MD from BWH and Harvard Medical School, will pave the way for new targets in the development of anti-inflammatory therapies.

The study is published in the May 24, 2012 online edition of The Journal of Clinical Investigation.

The researchers identified that expression of miR-181b was reduced in both mice and critically ill patients with sepsis. Sepsis is a devastating whole-body inflammatory condition due to infection and is associated with reduced survival.

Each one unit increase in microRNA-181b was associated with a decrease in the odds of having sepsis, suggesting that higher levels of miR-181b may be protective.

The inflammatory response (such as that which causes sepsis) is regulated by a major signaling pathway known as NF-kB. The researchers found that miR-181b is a potent regulator of this pathway

within blood vessel walls. miR-181b specifically targets importin-alpha3, a protein essential in NF-kB signaling.

Overexpression of miR-181b inhibited importin-alpha3 expression, as well as other molecules involved in the NF-kB signaling pathway; thereby, reducing the inflammation response.

The researchers discovered this after giving miR-181b intravenously in mice with sepsis. This led to increased survival and reduced inflammatory damage in the lungs of septic mice.

"We have discovered a microRNA that is important in dampening the inflammatory response and reducing tissue injury by targeting NF-kB in the lining of the blood vessel wall, known as the vascular endothelium," said Feinberg. "The beneficial role of this microRNA in sepsis is likely the tip of the iceberg since excessive inflammation is a pervasive finding in a wide-range of acute and chronic diseases."

In the accompanying commentary, Drs. Jason Fish and Myron Cybulsky from the University of Toronto note that microRNAs, such as miR-181b, may be exciting and attractive targets for future vascular inflammatory disease therapeutics.

Provided by Brigham and Women's Hospital