

# Leptin action in the brain linked to sepsis survival

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The hormone leptin, typically associated with body weight regulation, works within the central nervous system (CNS) to aid the immune system's defense against sepsis, researchers say.

Sepsis is a life-threatening medical condition in which the entire body is overwhelmed by infection.

A study led by Matthias Tschöp, MD, of UC's Metabolic Diseases Institute, and Charles Caldwell, PhD, of UC's surgery department, is the first to describe leptin's role in the control of immune response via the CNS. Results are published this week in the *Journal of Neuroscience*, the official journal of the Society for Neuroscience.

"Indirect evidence has previously indicated that the central nervous system might have a role in maintaining the immune system," says Tschöp. "For example, people with brain injuries appear to be at a higher risk for infection and sepsis. Sepsis is also a serious complication for stroke patients. What was lacking was any molecular mechanism to explain that relationship."

Researchers know that obesity causes an overproduction of leptin. High leptin levels make receptors "deaf" to the hormone, resulting in a loss of leptin function (leptin resistance) that leads to higher food intake.

Diet-induced obese mice have a survival advantage in sepsis. Because of this, the team hypothesized that leptin resistance, which is

seen at neurons regulating body weight, may not be happening at the brain centers that regulate the immune system.

To prove this, the team studied several leptin-deficient mouse models, including one that was missing leptin receptors everywhere except within the CNS. They report that leptin, long thought to act directly on [immune cells](#) themselves, also mediates actions in the CNS. They showed that leptin replacement improved the host response to a standard model of sepsis.

Leptin-dependent neurocircuitry, the authors say, is required for a proper immune response to sepsis, and damage to this circuitry, or even leptin deficiency, may lead to higher risk of death from sepsis.

"Human congenital leptin deficiency is rare," the authors say, "with less than a few dozen patients reported worldwide to date. But there is a stunning number of recorded cases of death due to [sepsis](#) in this patient population."

In addition, Tschöp says, this new finding gives researchers clues that could help in developing therapeutic targets for treating infection in people with damaged leptin-dependent neurocircuitry.

Provided by University of Cincinnati Academic Health Center

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