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Scientists discover immune system component that resists sepsis in mice

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Molecular microbiologists from the Keck School of Medicine of the University of Southern California (USC) have discovered that mice lacking a specific component of the immune system are completely resistant to sepsis, a potentially fatal complication of infection. The discovery suggests that blocking this immune system component may help reduce inflammation in human autoimmune and hyper-inflammatory diseases such as rheumatoid arthritis and Type 2 diabetes.

The study was published online on June 23 in *The Journal of Experimental Medicine*, a leading peer-reviewed scientific journal in research medicine and immunology.

The immune system is the body's first line of defense against infection. The system, however, can also injure the body if it is not turned off after the infection is destroyed, or if it is turned on when there is no infection at all. Scientists do not yet fully understand how the immune response is turned on and off and continue to study it in hopes of harnessing its power to cure disease.

In this study, scientists have found that a component of the system, HOIL-1L, is necessary for formation of the NLRP3-ASC inflammasome signaling complex.

"This regulatory mechanism is critical in vivo, where we find that mice lacking HOIL-1L are completely resistant to sepsis, which is a lethal inflammation model of human sepsis," said Mary Rodgers, Ph.D., USC

postdoctoral fellow and the study's first author. "Our results suggest that blocking the activity of HOIL-1L could be a new therapeutic strategy for reducing inflammation in disease."

More information: Rodgers, M. A., Bowman, J. W., Fujita, H., Orazio, N., Shi, M., Liang, Q. … Jung, J. U. (2014). The linear ubiquitin assembly complex (LUBAC) is essential for NLRP3 inflammasome activation. The *Journal of Experimental Medicine*, 1-15. Published online June 23, 2014; DOI: 10.1084/jem.20132486

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