Study shows novel way to study human inflammatory disease

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A new University of Colorado at Boulder study shows mice infected with the bacteria salmonella develop clinical signs consistent with a deadly and poorly understood human inflammatory disease, a finding that may lead to new therapies.

The human disease, known as Hemophagocytic Lymphohistiocytosis, or HLH, is a rare inflammatory disease that kills between 50 percent and 90 percent of its victims, said Diane Brown, lead author of the study. HLH treatment may require bone marrow transplantation, a drastic therapy with life-long consequences, according to Brown, adjoint curator at the University of Colorado Museum of Natural History.

The disease, in which the immune system becomes hyperactivated, occurs both in an inherited form, known as primary HLH, and in people with no known genetic defect, known as secondary HLH. Both forms are usually triggered by infections. The genetic form of HLH most often strikes infants and very young children.

A paper on the subject is being published Feb. 26 in PLoS One, a journal of the Public Library of Science. Study co-authors, all from CU-Boulder's molecular, cellular and developmental biology department, included Assistant Professor Corrella Detweiler, postdoctoral fellows Melissa McCoy and Carolina Pilonieta, and former master's student Rebecca Nix, now at Supergen in Salt Lake City. The study was funded by the National Institutes of Health and the American Recovery and Relief Act.

Salmonella is a well-known food contaminant, causing a variety of gastrointestinal tract symptoms in humans. While mice infected with salmonella are spared the cramping and diarrhea that humans develop, they were shown to develop a disease syndrome comparable to human secondary HLH, said Brown.

The CU-Boulder research team found that mice infected with salmonella developed fever, enlarged spleens, anemia, reduced numbers of platelets, dangerously high blood levels of an iron-storage protein, and neurological signs. In addition, specialized white blood cells known as hemophagocytic macrophages accumulated in the organs of the body, including bone marrow.

The team previously showed that salmonella-infected mice developed hemophagocytic macrophages, which ingest other white and red blood cells. "These earlier findings helped lead us down the current research path," said Detweiler.

"One part of this study is to try to use our research to understand how anemia develops in these infected mice, which might help us understand how symptoms of HLH develop," said Detweiler. The syndrome can be difficult to recognize and diagnose, she added.

"The availability of this animal model for HLH will help to advance the research and understanding of the underlying mechanisms of this immune system disorder," said Detweiler. "It also should provide a means to test new therapies for HLH."

Provided by University of Colorado at Boulder