Friday, June 1, 2018

Jaydev Upponi, Ph.D.

Science Editor of Immunology and Infection, *JOVE*

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Dear Dr. Upponi,

As per our email discussions we hereby submit to *JOVE* our manuscript titled, “**Neonatal polymicrobial sepsis: A guide for a controlled mouse model**.”

Human newborns are notably susceptible to infections in early life, and sepsis is one of the leading causes of death in this vulnerable population. Understanding disease in this group, and development of effective therapeutics has not been as impactful as work in other age groups, partly because neonatal sepsis is difficult to study in human newborns due to major limitation of sampling small volumes of blood as well as the rapid changes that occur in early life. As an adjunct strategy to investigate the mechanisms and test possible interventions, several animal models have been proposed, including a mouse model of neonatal sepsis (all references are provided in our manuscript). While neonatal mouse sepsis models, similar to the human, also are subject to inter-individual variability, they offer the distinct advantage of allowing standardization of the model to be implemented.

We here report our rigorous approach to standardize methods used to induce sepsis in neonatal mice. This guide will serve not only the larger community working on neonatal sepsis, but all who work with neonatal mouse models, as they provide a detailed range of assessments of the health/illness of newborn mice undergoing experimentation. Specifically, we provide the data supporting the development of an objective a humane endpoint that accurately identifies mice that would not otherwise recover from disease. We also present data showing that the traditional parameters used, such as weight change are not sufficient to separate mice that would recover from those that would not recover. This data-driven humane endpoint will greatly reduce animal suffering, without impacting the ability to experimentally study early life events.

This manuscript has not been published before, has only being submitted to JOVE, and will not be submitted elsewhere during the review process. If the manuscript is published then we will not publish it elsewhere in either similar form or verbatim without express written permission from the editors. The listed authors were involved with the conceptual development, design, interpretation, recording, drafting or revising of the manuscript and video, and have approved the manuscript.

If there is anything else we could to do help in the submission process, please do not hesitate to let us know.

Sincerely,



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