Mouse model suggests proteins cause damage in fetal abdominal inflammation

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Inflammation of the abdominal cavity in human fetuses resulting from a perforation of their intestine is likely to be caused by proteins contained in the fetal stool. This is the result of a Kobe University study that

established a new mouse model allowing research and drug development for a condition that is otherwise difficult to approach.

The fetus's stool, called the "meconium," is sterile but nevertheless causes inflammation of the abdominal cavity when it leaks out of the intestine after a perforation. Called "meconium peritonitis," this is a life-threatening condition for the baby with a mortality rate of 10–15% in humans, and neither a cause nor a treatment have been established.

The Kobe University pediatrician Fujioka Kazumichi and his team therefore decided to replicate the condition in mice.

Since the intestinal development of mice and humans is different, the intestine of a newborn mouse pup is equivalent to that of a human fetus after the 12th week of pregnancy, but even so, the mouse pup is too small and fragile to induce the condition through an operation.

The research team therefore created a slurry of meconium, which they took from human newborns, and injected it into the abdominal cavity of the pups. They then characterized the resulting condition and compared the pups' mortality rates in response to different treatments.

Their results, published in the journal *Pediatric Research*, show that mortality was not influenced by antibiotic treatment, ruling out a bacterial cause. However, when they heat-treated the meconium slurry before injection, which disrupts the natural shapes of proteins, they found a significant reduction in mortality.

This indicates that proteins contained in the meconium are responsible for the inflammation and, in particular, the archers assume digestive enzymes that are abundant in the meconium to be the culprits.

The Kobe University development has more general implications, too. In

a different set of experiments, Fujioka and his team characterized the condition of the mice pups after the meconium slurry administration by analyzing the mice's biochemical and gene expression profiles.

Comparing that to the results of a previously established mouse model, where the pups were injected with an extract of intestinal contents from adult mice, they could show that their model results in different symptoms.

Believing that their model is thus likely to be specific to meconium-caused inflammation, the researchers argue that it is an apt platform to conduct more research on the condition.

Fujioka and his team hope that their work will enable the search for an effective treatment of the condition, which occurs in about one out of every 35,000 live births.

They conclude, "As our mouse model is simple and highly reproducible, it can be used in research to elucidate the pathophysiology of meconium peritonitis."

More information: M. Ashina et al, A neonatal mouse model of meconium peritonitis generated using human meconium slurry, *Pediatric Research* (2024). DOI: 10.1038/s41390-024-03470-3. www.nature.com/articles/s41390-024-03470-3

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