Study finds gut microbiota influence severity of respiratory viral infection

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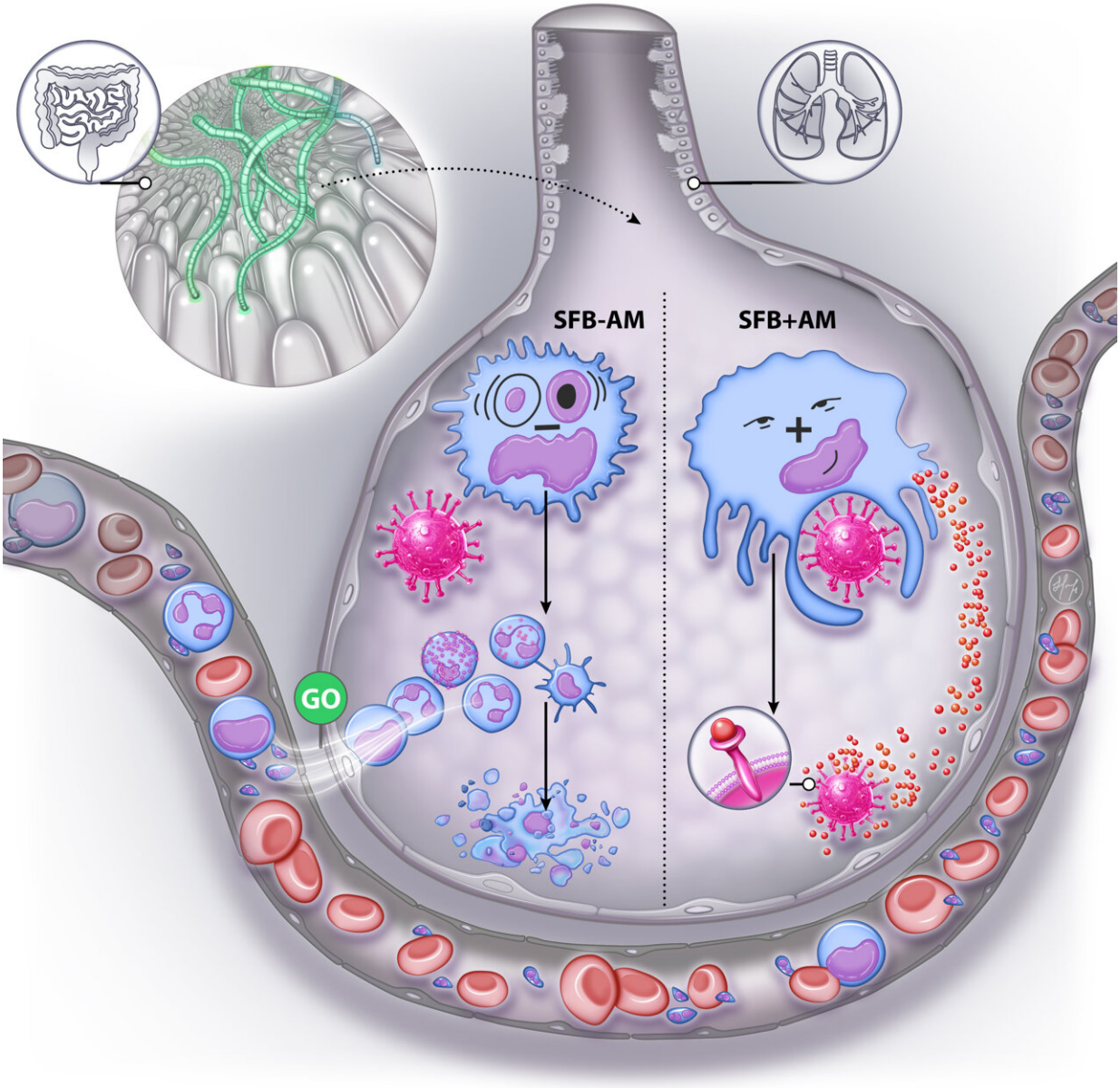

This picture illustrates an example of gut microbiota composition dictating how resident lung alveolar macrophages (AM) respond to viral infection. The presence of segmented filamentous bacteria, a commensal microbe present in some mice, reprograms AM gene expression, increasing complement expression and phagocytosis, thereby enabling AM to engulf and destroy viral pathogens without inflammatory signaling. Credit: Dr. Andrew Gewirtz

The composition of microbiota found in the gut influences how susceptible mice are to respiratory virus infections and the severity of these infections, according to researchers from the Center for Translational Antiviral Research in the Institute for Biomedical Sciences at Georgia State University.

The findings, published in the journal *Cell Host & Microbe*, report that segmented filamentous bacteria, a bacterial species found in the intestines, protected mice against influenza virus infection when these bacteria were either naturally acquired or administered.

This protection against infection also applied to respiratory syncytial virus (RSV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19. To maintain this protection, the study noted that segmented filamentous bacteria required immune cells in the lungs called basally resident alveolar macrophages.

In this study, the researchers investigated how differences in specific microbial species can impact outcomes of respiratory virus infections and how they might do so, which hasn't been well defined previously. They studied mice with discrete microbiome differences and mice differing in only the presence or absence of segmented filamentous bacteria. Viral titers in the lung were measured several days after infection and varied significantly depending on the nature of the

microbiome of the different animal groups.

"These findings uncover complex interactions that mechanistically link the intestinal microbiota with the functionality of basally resident alveolar macrophages and severity of respiratory virus infection," said Dr. Andrew Gewirtz, co-senior author of the study and Regents' Professor in the Institute for Biomedical Sciences at Georgia State.

The study found that in segmented filamentous bacteria-negative mice, basally resident alveolar macrophages were quickly depleted as respiratory virus infection progressed. However, in segmented filamentous bacteria-colonized mice, basally resident alveolar macrophages were altered to resist influenza virus infection depletion and inflammatory signaling.

The basally resident alveolar macrophages disabled influenza virus, in large part by activating a component of the immune system referred to as the complement system.

"We find it remarkable that the presence of a single common commensal bacterial species, amidst the thousands of different microbial species that inhabit the mouse gut, had such strong impacts in respiratory virus infection models and that such impacts were largely attributable to reprogramming of basally resident alveolar macrophages," said Dr. Richard Plemper, co-senior author of the study, Regents' Professor and director of the Center for Translational Antiviral Research at Georgia State.

"If applicable to human infections, these findings will have major implications for the future risk assessment of a patient to advance to severe disease."

"We find it highly unlikely that segmented filamentous bacteria is the

only gut microbe capable of impacting the phenotype of alveolar macrophages, and consequently, proneness to respiratory virus infection," Gewirtz said.

"Rather, we hypothesize that gut microbiota composition broadly influences proneness to respiratory virus infection. Microbiota mediated programming of basally resident alveolar macrophages may not only influence the severity of acute respiratory virus infection, but may also be a long-term post-respiratory virus infection health determinant."

The study's primary authors were virologist Carolin M. Lieber from the Center for Translational Antiviral Research and immunologist Vu L. Ngo from the Institute for Biomedical Sciences at Georgia State. Other contributing authors were Hae-ji Kang and Michal Kuczma of the Institute for Biomedical Sciences at Georgia State and Kaori Sakamoto of the University of Georgia.

More information: Intestinal microbiota programming of alveolar macrophages influences severity of respiratory viral infection, *Cell Host & Microbe* (2024). DOI: 10.1016/j.chom.2024.01.002. www.cell.com/cell-host-microbe … 1931-3128(24)00006-4

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