

Mother's blessing: Microbiota from mothers regulates lung immunity in newborns

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Microbiota from mothers regulates lung immunity in newborns. Credit: Helena Pinheiro, iMM



A new study led by Bruno Silva Santos, group leader and vice-director at the Instituto de Medicina Molecular João Lobo Antunes (iMM; Portugal), and published in *Cell Reports* revealed that a type of white blood cell, the $\gamma\delta$ T cell, influences the transfer of maternal microbiota during birth and nursing, and impacts the lung immune response in newborns.

Before birth, the lungs are filled with a sterile liquid that is replaced by gas in the first breath after birth, which causes an <u>immune reaction</u> involving substantial lung tissue remodeling, called "first breath response." Now, researchers at iMM implicated a specific type of immune cell, the $\gamma\delta$ T cell, in this immune response in mice.

"We found that newborns born and raised by mothers lacking $\gamma\delta$ T cells acquire a different gut <u>microbiota</u>. The intestinal microorganisms in these mice are not able to produce sufficient amounts of a type of molecules that are important to modulate the lung immune response to the first breath," explains the leader of the study, Bruno Silva Santos. "As result, these pups have an exacerbated first breath immune response."

The type of immune response that is induced after the first breath is also relevant in other contexts. The researchers observed a similar pattern in the progeny of mothers lacking $\gamma\delta$ T cells in response to an infection by a parasite that induces lung damage.

"We saw that either antibiotic treatment to kill the microorganisms in the gut, or supplementation with short-chain fatty acids, the molecules that are down in mice with exacerbated immune responses, abolish the differences between mice born from mothers with and without these immune cells. This shows that the effects observed in the pups are



indirect and linked to these molecules produced by the microbiota," adds Pedro Papotto, first author of the study which he initiated during his Ph.D. at iMM.

The complexity of the work takes another level on the transfer of microbiota from mothers to the newborns. "We found that the transfer of microorganisms from mothers is not restricted to the process of birth. If pups born from mothers lacking $\gamma\delta$ T lymphocytes are raised with mothers that have these cells, their <u>immune response</u> is restored. In fact, our study suggests that the majority of the bacterial communities must be transferred after birth, during nursing," explains Pedro Papotto.

It is already known that the developing immune system is sensitive to factors derived from mothers. Now, in this study, the researchers found that maternal $\gamma\delta$ T cells, which were never associated to this process, are involved in the development of the newborns lung immunity by exerting an effect in the gut microorganism's colonization. This also adds to the growing body of evidence on the physiological and therapeutic roles of the gut microbiota.

More information: Pedro H. Papotto et al, Maternal γδ T cells shape offspring pulmonary type 2 immunity in a microbiota-dependent manner, *Cell Reports* (2023). DOI: 10.1016/j.celrep.2023.112074

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