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What makes the newborn immune system in the lungs different and vulnerable?

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Newborns are more susceptible to infections, presumably because of their immature and inexperienced immune systems. The most common dangerous condition in newborns and infants are lower respiratory tract infections caused by viruses, especially respiratory syncytial virus (RSV). A study published on February 13th in *PLOS Pathogens* shows how the immune system in the lungs during early life differs from the one in older children and adults.

Ideally, newborns could be protected against RSV by vaccination, but it is known that the immune system in early life is less responsive to "conventional" vaccines. Barney Graham and colleagues, from the US National Institute of Allergy and Infectious Diseases, are working on understanding the early immune system in order to develop effective vaccines for newborns and infants.

The immune response to virus infection in the lung involves mobile immune cells called dendritic cells (or DCs). After contact with a viral intruder, the DCs move into adjacent lymph nodes where they activate another type of immune cell, called CD8+ T cells, and thereby orchestrate a massive, body-wide, virus-specific attack. Graham and colleagues studied the behavior of these lung DCs in newborn mice and compared it with that in older animals.

They found that the lung DC responses following RSV infection undergo dramatic changes during the first weeks of life. One of the two subsets active in adults was present in low numbers and functionally limited in

newborn mice. The second subset, called CD103+ DCs, is present in similar numbers in newborn and adults after virus infection. Following migration to the lymph nodes, CD103+ DCs initiate CD8+ T cell responses. However, when newborn CD103+ DCs and CD8+ T cells interact, the results are very different from the same interaction in older mice.

Depending on the age of the mice at the time of RSV infection, the CD103 DCs activate different subsets of CD8+ T cells. This suggests that DCs from newborns take up, digest, and present parts of an intruding virus to other immune cells in a fundamentally different way than in adults. In addition, the researchers found that CD103+ DCs from newborn mice have much lower expression of two critical "co-stimulatory" molecules (called CD80 and CD86) on their surface. These co-stimulators directly interact with a counterpart (called CD28) on the CD8+ T cells and in doing so boost the immune response, something that is severely impaired in neonatal mice. Dampening CD28-mediated stimulation in adult mice demonstrated that limited CD28-mediated co-stimulatory support from neonatal DCs may constitute one mechanism by which newborn and adult DCs induce distinct CD8+ T cell responses.

"A better understanding of deficiencies in early-life immunity will guide vaccine approaches that induce disease-sparing immune responses in infants", the researchers say. "Our data suggest that the CD80/CD86-CD28 axis may be exploited in the design of pediatric vaccines to promote the generation of more "adult-like" immune responses".

More information: Ruckwardt TJ, Malloy AMW, Morabito KM, Graham BS (2014) Quantitative and Qualitative Deficits in Neonatal Lung-Migratory Dendritic Cells Impact the Generation of the CD8+ T Cell Response. *PLoS Pathog* 10(2): e1003934. DOI: 10.1371/journal.ppat.1003934