Immunosuppressive cells in newborns play important role in controlling inflammation in early life

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New research led by The Wistar Institute, in collaboration with Sun Yat-sen University in China, has characterized the transitory presence of myeloid-derived suppressor cells (MDSCs) in mouse and human

newborns, revealing a critical role of these cells in regulation of inflammation in the early stages of life. This study was published online in *Nature Medicine*.

MDSCs are immature myeloid cells with the ability to suppress immune responses. In healthy adults, these cells are rarely detected but accumulate during certain pathological conditions, altering the immune response to cancer and chronic infection and promoting tumor progression.

"Our research sheds light on the function of MDSCs in newborns, suggesting that they are critical for the regulation of inflammation during the first weeks of life," said Dmitry I. Gabrilovich, M.D., Ph.D., Christopher M. Davis Professor and program leader of the Immunology, Microenvironment and Metastasis Program at Wistar. "We also revealed a physiological role of MDSCs expansion, which was widely considered to be driven by pathological conditions or pregnancy, broadening the importance of MDSCs in the immune system."

Gabrilovich and colleagues compared the proportion of MDSCs in newborn, adult and postpartum mice. Those that were three to 10 days old had substantially higher numbers of these cells with a potent immunosuppressive ability and the proportion gradually decreased to levels comparable to those in adult mice by the end of the second week of life.

Analyzing the transcription profile of MDSCs from newborn mice, the team observed increased expression of genes that are critical for the immunosuppressive functions of these cells. Mechanistically, they demonstrated that the accumulation of MDSCs is linked with milk feeding, as it depends on lactoferrin, a milk component with potent immunoregulatory activity, which can induce upregulation of these genes.

The researchers also found that MDSCs are important for the control of inflammation in newborns. In fact, human newborns with normal birth weight had significantly higher proportion of MDSCs and higher immunosuppressive activity compared with adults as well as infants with low birth weight. These infants are at a higher risk for development of pathological inflammatory conditions, such as necrotizing enterocolitis, a condition that causes inflammation of the intestine and may put the infant at risk for developing potentially life-threatening infections.

"Our findings demonstrate that MDSCs reduce inflammation and increase survival in a model of necrotizing enterocolitis, thus suggesting that MDSCs not only can be present in healthy individuals but also could be an important protection mechanism evolved in response to the microbial colonization of the gut that takes place during the first days of life," said Gabrilovich.

"Based on our data, MDSCs may be used as a potential therapeutic target for treating necrotizing enterocolitis and other inflammatory conditions in infants," said Michela Perego, Ph.D., an associate staff scientist in the Gabrilovich Lab and co-first author of the study. "Our finding that accumulation of MDSCs depends on lactoferrin may also provide a rationale as to why feeding infants human milk versus formula has been shown to reduce the risk of necrotizing enterocolitis."

More information: Transitory presence of myeloid-derived suppressor cells in neonates is critical for control of inflammation, *Nature Medicine* (2018). nature.com/articles/doi:10.1038/nm.4467

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