UKE Paper of the Month August 2021

Vertically transferred maternal microchimeric immune cells promote neonatal immunity against early life infections

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ABSTRACT: During mammalian pregnancy, immune cells are vertically transferred from mother to fetus. The functional role of these maternal microchimeric cells (MMc) in the offspring is mostly unknown. Here we show a mouse model in which MMc numbers are either normal or low, which enables functional assessment of MMc. We report a functional role of MMc in promoting fetal immune development. MMc induces preferential differentiation of hematopoietic stem cells in fetal bone marrow towards monocytes within the myeloid compartment. Neonatal mice with higher numbers of MMc and monocytes show enhanced resilience against cytomegalovirus infection. Similarly, higher numbers of MMc in human cord blood are linked to a lower number of respiratory infections during the first year of life. Our data highlight the importance of MMc in promoting fetal immune development, potentially averting the threats caused by early life exposure to pathogens.

STATEMENT:

The transfer of maternal cells to the fetus across the placenta during pregnancy is an evolutionary preserved phenomenon which has been known for a number of years. However, the functional role of these cells in fetal organs was still unknown. This is the first study to functionally investigate the role of maternal cells in the offspring using in preclinical models (mouse models) and to translate such findings into clinical relevance. We identified that maternal cells in the fetus increase neonatal immune defense mechanisms, i.e. when facing pathogens. In turn, maternal cells mitigate the risk for early life infections, as we have shown here in murine offspring as well as children born within the UKE-based PRINCE Study, a longitudinal pregnancy cohort. Due to the large array of methodological approaches and scientific expertise needed to address this complex research question, these findings arose from an interdisciplinary approach of individual´s based at several departments of the UKE.

BACKGROUND:

This work was performed at the Department of Obstetrics and Fetal Medicine in the Division for experimental Feto-Maternal Medicine in the group of Prof. Dr. Petra Arck, Professor for Experimental Feto-Maternal Medicine who has been recruited to the UKE in 2010. The recent publication was part of the PhD thesis of Dr. Ina A. Stelzer and part of the Bachelor thesis of Christopher Urbschat, who shared first authorship. It was supported by the German Research Foundation (KFO296). Both first authors have strong interests in reproductive immunology, how the immune system develops in utero and what determines immunological competence of the offspring later in life.