

IL-27 AND IMMUNOSUPPRESSION IN INFANTS

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Abstract

Background and Significance: Successful human pregnancy depends on the initiation and maintenance of local immunological tolerance to the semi-allogenic fetus. The immunosuppressive microenvironment at the fetal-maternal interface also regulates the fetal immune system and thus may at least be partially responsible for the immaturity of the neonatal immune system. The resultant deficiencies lead to a greater susceptibility to microbial infection, a major cause of mortality early in life. Studies in our laboratory have shown that human cord blood-derived macrophages express a higher level of interleukin (IL)-27 compared to adult macrophages. IL-27 has been shown to oppose inflammation and may be induced during pregnancy to regulate the maternal immune response to the fetus. To determine whether this elevated expression is maintained throughout infancy, we examined the expression of IL-27 throughout the murine life cycle along with possible mechanisms of immunosuppression.

Methods: Splens were harvested from C57BL/6 mice ($n = 6$) at different stages of life and homogenized for RNA isolation. Gene expression of both subunits of IL-27, EB13 and p28, was measured by real time PCR. To confirm gene expression levels, spleen-derived macrophages from mice ($n = 4$) were immunolabeled for IL-27 protein at three stages of life. Macrophage surface marker and intracellular IL-27 were concurrently labeled with fluorophore-conjugated specific antibodies for flow cytometry analysis.

Results: The relative gene expression of IL-27 in adult (day 56) mice was significantly lower than the expression in neonatal (day 8) mice. Similar results were found in human cord-blood derived macrophages, which express IL-27 at an elevated rate compared to adult macrophages. Age-dependent analysis of murine IL-27 gene expression throughout the mouse life cycle indicated that levels of IL-27 remain significantly elevated through infancy and adolescence. Flow cytometry analysis further confirmed these results, demonstrating that macrophage IL-27 protein levels are significantly higher in both neonate and infant mice compared to adult mice.

Discussion: The elevated expression of IL-27 throughout infancy in the mouse model indicates that increased levels of IL-27 may contribute to the immunosuppressive phenotype of neonatal macrophages. Thus susceptibility to infection that is observed throughout early life may be minimized by blocking IL-27. Progesterone directly induces transcription of IL-27 in a dose-responsive manner, which may be beneficial during pregnancy. However, the mechanism of continued elevated expression of IL-27 in infancy must be examined further.

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