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# **Potent Induction of IFN- $\gamma$ Production from Cord Blood NK Cells by the Stimulation with Single-Stranded RNA**

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## **Summary:**

The innate immune system is the first line of host defense mechanism against microbes, and the quality and magnitude of its reaction affect the subsequent adaptive immune responses. One of the reasons of increased susceptibility to the severe and recurrent viral infections in neonates than adults is more naive nature of T cells with reduced responsiveness to the stimulation of viral antigens. On the other hand, the extent of functional difference of innate immune response between neonates and adults is not known.

Natural killer (NK) cells play important roles in the innate immunity against viral infections. Although newborn infants are more susceptible to severe and recurrent viral infections than adults, the precise role of NK cells in the innate immunity against viral infections during neonatal period is not known. To clarify the functional characteristics of cord blood (CB) NK cells, we examined the capacity of CB NK cells to produce interferon gamma (IFN- $\gamma$ ) in response to the Toll-like receptor (TLR) ligands. We found that NK cells produced a large amount of IFN- $\gamma$  by the stimulation with ssRNA, a TLR8 ligand, in the presence of interleukin-2 (IL-2), Interferon alpha (INF- $\alpha$ ), and monocytes. Surprisingly, CB NK cells produced higher amount of IFN- $\gamma$  than adult peripheral blood NK cells in this

condition. IL-12 produced from monocytes by the stimulation with ssRNA was indispensable for the production of IFN- $\gamma$  by NK cells. NK cells in cooperation with other innate immune cells may play more important role during the neonatal period than in adults in the host defense against viral infections by high capacity of IFN- $\gamma$  production to compensate immature acquired immunity. In contrast to the immature acquired immune system in human neonates and infants, which is the cause of increased susceptibility to infections by a wide range of pathogens, innate immune system to produce IFN- $\gamma$  by NK cells may play more important role in them than adults in preventing viral pathogens in concert with accessory cells.