

UTERINE NK CELLS AND PREGNANCY

Introduction: Uterine Natural Killer cells are a subtype of NK cells with very distinct and important features, these features will give these cells functions that are essential in certain stages of development. The main difference between uterine NK cells and peripheral NK cells rests in their loss of cytotoxic activity and the production of cytokines that produces a favorable environment for pregnancy. These uNK cells are the most numerous leukocytes in early pregnancy.

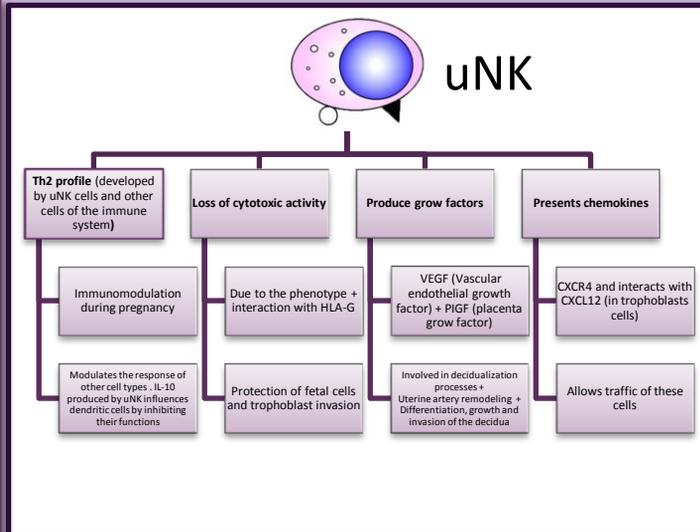
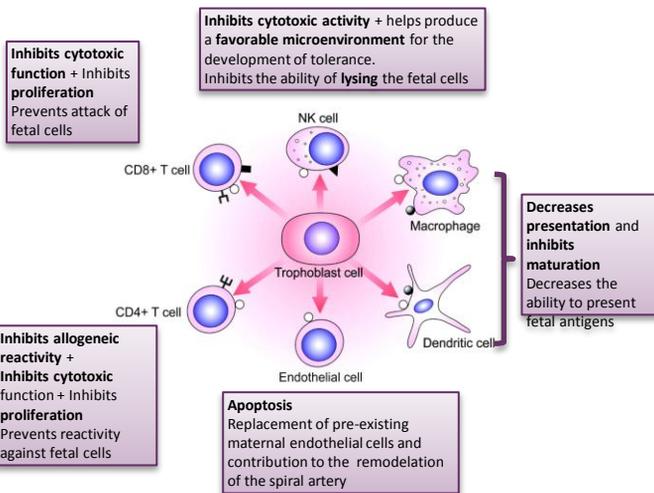
Methodology: Literature search in PubMed and webs of science. Selection of articles and literature reviews of recent years.

Uterine Natural Killer vs. Peripheral Natural Killer

	uNK	pNK
Abundance	70% of human decidua	10-25% of lymphocytes in blood
Origin	Presence in the decidua: Homing from peripheral blood because of interaction with the endothelial cell adhesion molecules Proliferation and differentiation in situ	Bone marrow stem cells Dependent differentiation: SCF, IL-15, IL-7
Receptors	CD56 ^{Bright}  → They do not express the activator receptor.	CD56 ^{Bright} CD16 ^{dim} (1%) CD56 ^{dim} CD16 ^{Bright} (99%)
Functions	Invasion of the extravillous trophoblast. It will penetrate into the maternal's decidua and the miometrium. Remodeling of the uterine spiral arteries.	Innate response. Response against intracellular pathogens, the most common viral infections. Regulation of adaptive responses and hematopoiesis

Action of HLA-G in trophoblasts cells

Action of uNK cells during pregnancy



Interaction of HLA-G present in trophoblast cells with different immune cells present in the pregnancy decidua. Hunt, et al. 2005. HLA-G and immune tolerance in pregnancy (review). The FASEB Journal. Vol.19, 681-693. (modified image).

Successful pregnancy

Conclusions:

- Clear evidence of a subset of NK cells, NK decidual cells, with specific and different characteristics. One of the most important features is the loss of the cytotoxic capacity and the modulation of the environment with cytokines.
- Important role in the development of pregnancy by promoting trophoblast invasion and spiral artery remodeling.
- The HLA-G present in trophoblast causes immunomodulatory action in different cell populations and inhibits usual functions in these cells compared to other tissues and other environments.
- The interaction of HLA-G with uNK particularly, contributes to the production of a favorable microenvironment tissue tolerance and inhibition of cytotoxic activity.
- The interaction with HLA-G and the microenvironment (profile Th2) generated by uNK cells prevent rejection of pregnancy.

References:

1. Chrysoula Dosi and Linda C. Giudice. 2005. Natural Killer Cells in Pregnancy and Recurrent Pregnancy Loss: Endocrine and Immunologic Perspectives. Endocrine Reviews, 26(1): 44-62.
2. Szekeres-Bartho, J. Symposium: Current Knowledge on natural killer cells, pregnancy and pre-eclampsia. Regulation of NK cell cytotoxicity during pregnancy. 2008. Reproductive BioMedicine Online. Vol 16 No 2. 211-217.
3. Genevieve Eastbrook, BSc, MD, Yuxiang Hu, MSc, Peter von Dadelzen, MB, ChB, DPHI, FRCS. The role of Decidual Natural Killer Cells in Normal Placentation and in the Pathogenesis of Preeclampsia. 2008. Obstetrics 30(6): 467-476.
4. G.E Lash, S.C Robson, J.N Bulmer. 2010. Review: Functional role of uterine natural killer (uNK) cells in human early pregnancy decidua. Placenta 31, Vol.26, 97-99.