**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.

**Metodology:** Literature search in PubMed and web of science. Selection of articles and literature reviews of recent years.

### Uterine Natural Killer vs. Peripheral Natural Killer

<table>
<thead>
<tr>
<th></th>
<th>uNK</th>
<th>pNK</th>
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<tbody>
<tr>
<td><strong>Abundance</strong></td>
<td>70% of human decidua</td>
<td>10-25% of lymphocytes in blood</td>
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<tr>
<td><strong>Origin</strong></td>
<td>Presence in the decidua: Homing from peripheral blood because of interaction with the endothelial cell adhesion molecules</td>
<td>Bone marrow stem cells: Dependent differentiation: SCF, IL-15, IL-7</td>
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<tr>
<td><strong>Receptors</strong></td>
<td>CD56bright</td>
<td>CD56dim (1%), CD56dim (99%)</td>
</tr>
<tr>
<td><strong>Functions</strong></td>
<td>Invasion of extravillus trophoblast. It will penetrate into the maternal's decidual and the miometrium. Remodeling of the uterine spiral arteries.</td>
<td>Innate response: Response against intracellular pathogens, the most common viral infections. Regulation of adaptive responses and hematopoiesis</td>
</tr>
</tbody>
</table>

### Action of HLA-G in trophoblasts cells

- Inhibits cytotoxic activity + helps produce a favorable microenvironment for the development of tolerance.
- Inhibits the ability of lysing the fetal cells
- Prevents reaction against fetal cells
- Inhibits allogenic reactivity + inhibits proliferation
- Prevents reaction against fetal cells
- Apoptosis: Replacement of pre-existing maternal endothelial cells and contribution to the remodeling of the spiral artery

### Action of uNK cells during pregnancy

- TH2 profile (developed by uNK cells and other cells of the immune system)
- Loss of cytotoxic activity
- Produce growth factors
- Protects fetal cells and trophoblast invasion
- Modulates the response of other cells types: A-13 produced by uNK influences dendritic cells by inhibiting their functions
- Due to the phenotype + Interaction with HLA-G
- VEGF (Vascular endothelial growth factor) = PGF (placenta growth factor)
- Involved in desialylation process: uNK cells are remodeling the decidua
- EDC4A and interacts with CXCR4 (to trophoblasts cells)
- Allows traffic of these cells
- Presents chemokines

### References:

### 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 trophoblasts 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.