



## The Major Role of Natural Killer Cells in Cancer Immunology and Reproductive Medicine

**Ioannis K Toliopoulos\***

*Konstantinon Research Center of Molecular Medicine and Biotechnology, Thessaloniki, Greece*

**\*Corresponding Author:** Ioannis K Toliopoulos, Konstantinon Research Center of Molecular Medicine and Biotechnology, Thessaloniki, Greece.

**Received:** January 05, 2018; **Published:** January 09, 2018

The discovery of NK cells in more than 30 years ago, open a new era in immunology and specifically in cancer immunology and reproductive immunology. Many studies have been taken place in medicine in order to obtain new diagnostic panels and therapeutic strategies involving NK cells.

In cancer, it has been reported that the number of NK cells and their activity is decreased especially in cancer patients with solid tumors [1,2]. Different research projects suggest that a role of T lymphocytes might be significant in tumour development [3]. iNKT cells are a new subpopulation of T cells and show cytotoxic activity against tumours [4]. After activation, NK cells also secrete several cytokines such as interferon- $\gamma$  (IFN- $\gamma$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), granulocyte macrophage colony-stimulating factor (GM-CSF), and chemokines (CCL1, CCL2, CCL3, CCL4, CCL5, and CXCL8) that can modulate the function of other innate and adaptive immune cells [5]. Also, several studies point out that apart from the NK cell cytotoxic function, the cytokines, which are secreted by the NK cells also provide a significant boost to the antitumor immunity. Similarly, the cytokines secreted by other immune cells or stromal cells in the tumor microenvironment can positively or negatively influence the antitumor function of NK cells [6,7]. Furthermore, studies concerning stimulation of NK cells have been performed by natural methods (administration of plant extracts and low frequency electromagnetic fields) without side effects and assisted in good quality of life in cancer patients with solid tumors [8].

On the other hand, the role of NK cells is totally different in reproductive medicine and unique. The high number of the NK cells and as well as the activity is associated with the unexplained infertility, rapid spontaneous abortions (RSAs), and failed IVFs.

High NK cell activity has been associated with miscarriage and embryo implantation failure, because these cells attack the embryo in its early development in the uterus and recognize as a foreign body. Further randomised trials are clearly needed to prove that treatment leads to better pregnancy outcomes. However, the results of the research to date are promising, and there are exciting possibilities for the future.

Scientists, nowadays know that the NK cell population found in the uterine endometrium and in the decidua (typically CD16 negative, CD56 bright) are both phenotypically and functionally different from those NK cells in the peripheral circulation (typically CD16+, CD56 dim). However, Fukui, *et al.* have shown a significant increase in the percentage of endometrial CD16+ CD56dim peripheral blood type NK cells in women who failed IVF and embryo transfer compared to those who were successful [9]. Additionally, Chaouat, *et al.* have shown peripheral blood NK cells to produce embryotoxic levels of Th1 type cytokines when stimulated with a trophoblast antigen extract. Thus, some of the NK cells that accumulate at the site of implantation are potentially of peripheral blood origin and are capable of damaging trophoblastic cells [10].

However, professional provisional work does suggest that therapy aimed at reducing NK cell activation leads to an improved outcome of IVF treatment and prevent miscarriages [11]. Indeed glucocorticoids may be helpful in reproductive medicine or recurrent idiopathic failed IVF precisely because they can inhibit the production of Th1 type cytokines and encourage Th2 type cytokines by antigen presenting cells and T helper cells [12]. Distinguished doctors in reproductive immunology treat women with NK problem for more than 30 years with targeted individual therapies based on intralipid and IVIg and handle successfully unexplained infertility, miscarriages, and failed IVFs [13].

Conclusively, NK cells are vital cells in assisting for new life in reproductive medicine and in saving a life in cancer patients and therefore should be considered as a prognostic and diagnostic tool in daily routine by professional scientists.

### Bibliography

1. Claus M and Watzl C. "Evaluation of human natural killer cell activities in whole blood". *Current Protocols in Immunology* Chapter 7 (2010): Unit7.39.
2. Terabe M and Berzofsky JA. "The immunoregulatory role of type I and type II NKT cells in cancer and other diseases". *Cancer Immunology, Immunotherapy* 63.3 (2014): 199-213.
3. Kardasz-Ziomek M, *et al.* "Long term results of partial laryngectomies in patients suffering from laryngeal cancer". *Otolaryngologia Polska* 66.1 (2012): 46-50.
4. Klatka J, *et al.* "The percentage of iNKT cells among other immune cells at various clinical stages of laryngeal cancer". *Postepy Higieny I Medycyny Doswiadczalnej* 70 (2016): 392-399.
5. Carrega P and Ferlazzo G. "Natural killer cell distribution and trafficking in human tissues". *Frontiers in Immunology* 3 (2012): 347.
6. Frederiksen KS, *et al.* "IL-21 induces in vivo immune activation of NK cells and CD8(+) T cells in patients with metastatic melanoma and renal cell carcinoma". *Cancer Immunology, Immunotherapy* 57.10 (2008): 1439-1449.
7. Cai G, *et al.* "IL-10 enhances NK cell proliferation, cytotoxicity and production of IFN-gamma when combined with IL-18". *European Journal of Immunology* 29.9 (1999): 2658-2665.
8. Angelos Evangelou, *et al.* "Functionality of natural killer cells from end-stage cancer patients exposed to coherent electromagnetic fields". *Electromagnetic Biology and Medicine* 30.1 (2011): 46-56.
9. Fukui A, *et al.* "Natural killer cell subpopulations and cytotoxicity for infertile patients undergoing in vitro fertilization". *American Journal of Reproductive Immunology* 41.6 (1999): 413-422.
10. Chaouat G, *et al.* "TH1/TH2 paradigm in pregnancy: paradigm lost? Cytokines in pregnancy/early abortion: reexamining the TH1/TH2 paradigm". *International Archives of Allergy and Immunology* 134.2 (2004): 93-119.
11. Coulam CB and Roussev RG. "Correlation of NK cell activation and inhibition markers with NK cytotoxicity among women experiencing immunologic implantation failure after in vitro fertilization and embryo transfer". *Journal of Assisted Reproduction and Genetics* 20.2 (2003): 58-62.
12. Elenkov IJ. "Glucocorticoids and the Th1/Th2 balance". *Annals of the New York Academy of Sciences* 1024 (2004): 138-146.
13. RG Roussev, *et al.* "Laboratory Evaluation of Women Experiencing Reproductive Failure". *American Journal of Reproductive Immunology* 35.4 (1996): 415-420.

**Volume 2 Issue 1 January 2018**

© All rights are reserved by Ioannis K Toliopoulos.