# **ImmunoTools** *special* Award 2014

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## Study of the immunological quality of the endometrium in different reproductive pathologies

Infertility is a growing problem worldwide wich affects 9% of couples on reproductive age. Pregnancy rate has been increased by assisted reproductive techniques (ART) mainly through the development of new methods of culture, selection and transfer of gametes and embryos. However, the function and endometrial receptivity have agreed to be the main limiting factors in the establishment of pregnancy. In this sense, innovation to detect endometrial dysfunction should be developed. In this sense, we propose R&D lines to stablish immunological markers of infertility in the endometrium of reproductive failure patients.

Available evidence regarding the immunological processes determining uterine receptivity indicates that uterine natural killer cells (uNK) must be activated for the appropriate production of angiogenic and immunotrophic cytokines. In addition, some of the main cytokines produced by activated NK cells, including IFN-gamma and TNF-alpha, have been associated with the recurrent spontaneous abortion and implantation failure. Testing of these markers may allow to suggest adecuate and personalized immunomodulatory treatment.

For this purpose is necessary to stablish normal values of each immunomarker by using antibodies to specific clusters of differentiation (CD). These proteins include CD3, CD4, CD8, CD19, CD5, CD56, CD16, CD25, and CD45. $CD4^+$ T cells are a type of $CD3^+$ T lymphocytes which are the directors of the immune response, since they guide immune responses towards distinct subsets of T helper (Th) cells from *naïve* Th0 cells into Th1, Th2, Th17, or Treg cells. $CD4^+CD25^+Foxp3^+$ Treg cells have recently been implicated in human

pregnancy as key players in protecting the embryo from alloreactive immune rejection. On the other hand, $CD19^+$ $CD5^+$ lymphocytes (LB1 cells) are frequently elevated in women with an autoimmune factors associated to their infertility.

On the other hand, cytokines are small multifunctional glycoproteins, whose biological actions are mediated by specific cell surface receptors and intracellular signaling as act as potent regulators of the functions of the endometrial cells and embryo-maternal interactions. Interleukin (IL)-6 is a cytokine capable of modulating the quality of the immune response during implantation and gestation; deficient levels are associated with implantation failure, while exacerbated levels have been associated with recurrent abortions, preterm delivery and preeclampsia. Transforming Growing Factor (TGF)-beta may play a key role in human implantation via the stimulation of fibronectin or Vascular Endothelial Growth Factor (VEGF). Granulocyte-Colony Stimulating Factor (G-CSF) also contributes to human reproductive success. It appears to be essential for implantation and it deficiency is associated to recurrent pregnancy loss.

Taking all these into account, ImmunoTools reagents could help us to determine uterine and systemic levels of NK cells, Treg cells, LB1 cells, T cells, IL-6, IL-8, G-CSF, IFN-gamma and TNF-alpha during the implantation window, providing new biomarkers for the diagnosis of immunological factors in unexplained infertility and allowing Medical Doctors to find new therapeutic options.

**ImmunoTools** *special* AWARD for **Gisela Junovich** includes 22 reagents

FITC - conjugated anti-human CD3, CD5, CD9, CD25, Control-IgG1,
PE - conjugated anti-human CD56, CD61, Control-IgG1,
PerCP - conjugated anti-human CD8, CD45,
APC -conjugated anti-human CD4, CD16, CD19, CD69, Control-IgG1,
recombinant human cytokines rh IFN-gamma, rh TNF-alpha, rh TGF-beta, rh G-CSF,
human IL-6 ELISA-set, human TNF-alpha ELISA-set, human IL-8 ELISA-set