



Universiteit
Leiden
The Netherlands

Unsupervised analysis approach reveals increased endometrial NKp30 frequency in patients with idiopathic RPL

Gurbanova, A.; Feyaerts, D.; Benner, M.; Heijden, O.W.H. van der; Hoorn, M.L. van der; Joosten, I.; ... ; Molen, R.G. van der

Citation

Gurbanova, A., Feyaerts, D., Benner, M., Heijden, O. W. H. van der, Hoorn, M. L. van der, Joosten, I., ... Molen, R. G. van der. (2023). Unsupervised analysis approach reveals increased endometrial NKp30 frequency in patients with idiopathic RPL. *Journal Of Reproductive Immunology*, 158. doi:10.1016/j.jri.2022.103601

Version: Publisher's Version

License: [Creative Commons CC BY 4.0 license](https://creativecommons.org/licenses/by/4.0/)

Downloaded from: <https://hdl.handle.net/1887/3728601>

Note: To cite this publication please use the final published version (if applicable).

protein expression of IL-1 β and IL-18 was examined by immunohistochemical staining in the decidua of healthy pregnancies (n = 15), spontaneous miscarriage (SM) (n = 18) and RM (n = 15). Double-immunofluorescence was carried out for the characterization of IL-1 β and IL-18 expressing cells in the decidua.

Results: Gene expression analysis revealed an overexpression of IL-1 β and IL-18 in RMPatients. IL-18 protein expression was significantly upregulated in the decidua of the RMgroup (p = 0.031). In SM specimens there was no significant difference in IL-18 expression when compared to healthy controls (p=0.172). Immunohistochemical staining showed a significant elevated expression of IL-1 β in the decidua of RM (p = 0.01) and SM patients (p = 0.001) in comparison to the control group. Double-immunofluorescence identified decidual stroma cells as IL-1 β and IL-18 expressing cells.

Conclusion: IL-1 β expression is significantly elevated in the decidua in both miscarriage groups and IL-18 upregulation is restricted to RM patients. The overexpression of IL-1 β and IL-18 might lead to or may be a result of a pro-inflammatory immune response at the fetomaternal interphase and could consequently induce miscarriage. The secretion of both cytokines is stimulated by the activated inflammasome NLRP3 (NOD-, LRR- and pyrin domain containing 3) and the inhibition of this upstream might be a new therapeutic approach for miscarriage patients

<http://dx.doi.org/10.1016/j.jri.2022.103600>

POSTER 18

Unsupervised analysis approach reveals increased endometrial NKp30 frequency in patients with idiopathic RPL

Aysel Gurbanova^{a,11}, Dorien Feytaerts^{a,11,12}, Marilen Benner^a, Olivier WH van der Heijden^b, Marie-Louise van der Hoorn^c, Irma Joosten^a, Gerben Ferwerda^a, Marien de Jonge^a, Renate G van der Molen^a

^a Department of Laboratory Medicine, Laboratory of Medical Immunology, Radboud University Medical Center, Nijmegen, The Netherlands

^b Department of Obstetrics and Gynaecology, Radboud University Medical Center, Nijmegen, The Netherlands

^c Department of Gynaecology and Obstetrics, Leiden University Medical Center, Leiden, The Netherlands

Problem: Worldwide, 1-4% of all women who conceive suffer from recurrent pregnancy loss (RPL). Over 50% of these cases have no identified risk factor and are called idiopathic RPL. It is known that the immunological balance between inflammation and tolerance in the uterine microenvironment is crucial for achieving a successful pregnancy. Natural Killer (NK) cells are abundantly present locally and with their cytotoxic and inhibitory functions, they are thought to be the main regulator of the processes behind implantation and decidualization. To understand in more detail the role of NK cells in RPL we have investigated the receptor repertoire of NK cells in both menstrual blood (MB) and peripheral blood (PB) of women with a history of RPL and healthy pregnancy.

Method of Study: Menstrual and peripheral blood samples were collected from women with 3 or more unexplained RPL (n=17) and healthy controls (n=13). Isolated cells were stained with comprehensive NK cell panels and analyzed with multi-color flow cytometry. Alongside traditional gating methods, unsupervised machine learning methods were applied to investigate the immune landscape of NK cells.

¹¹ Authors contributed equally.

¹² **Present address:** Stanford University School of Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford, CA, USA.

Results: Unsupervised analysis demonstrated a significant difference in the NK cell landscape of RPL patients compared to the control group. First the ratio of CD56Bright (CD3-CD56 + CD16-) to CD56Dim (CD3-CD56 + CD16+) cells was lower in menstrual blood of RPL patients indicating a higher frequency of CD56Dim cells. Based on the clustering algorithm, we additionally observed changes in the clusters expressing Natural Cytotoxicity Receptors (NCRs) mainly NKp30. With a manual gating strategy, we confirmed a significant increase in the frequency of NKp30 + receptor and combination of NKp30 + NKp44 + receptor cells in RPL patients. Currently, we are investigating the NK cell repertoire in a new cohort idiopathic RPL patients.

Conclusion: As a main regulator in the uterine immune system, a comprehensive analysis of the NK cell immune landscape can give insight into the mechanism behind idiopathic RPL. With an unsupervised data analysis method, we can reveal the subtle differences in an unbiased fashion which is not possible with traditional gating methods. Based on this method, we can discover biomarkers involved with RPL occurrence.

Preeclampsia

<http://dx.doi.org/10.1016/j.jri.2022.103601>

POSTER 19

Regulation of epigenetic modifications in the placenta during preeclampsia: PPAR γ influences H3K4me3 and H3K9ac in extravillous trophoblast cells

Sarah Meister^{1,*,13}, Laura Hahn^{1,14}, Susanne Beyer^{1,15}, Corinna Paul^{1,16}, Sophie Mitter^{1,17}, Christina Kuhn^{2,18}, Viktoria von Schönfeldt^{1,19}, Stefanie Corradini^{3,20}, Kritika Sudan^{4,21}, Christian Schulz^{4,22}, Theresa Maria Kolben^{1,23}, Sven Mahner^{1,24}, Udo Jeschke^{1,2,*,25}, Thomas Kolben^{1,26}

¹ Department of Gynecology and Obstetrics, University Hospital, LMU Munich, Marchioninistr. 15, 81377 Munich, Germany

² Department of Gynecology and Obstetrics, University Hospital Augsburg, 86156 Augsburg, Germany

³ Department of Radiation Oncology, University Hospital, LMU Munich, Marchioninistr. 15, 81377 Munich, Germany

⁴ Medizinische Klinik und Poliklinik I, Klinikum der Universität München LMU Munich, Marchioninistr. 15, 81377 Munich, Germany

Problem: Preeclampsia is a severe pregnancy disorder with high mortality and morbidity. The only known curative therapy is the delivery of the baby. Therefore, gaining knowledge of the

*Corresponding authors. Tel.: +49-89-4400-54266; Fax: +49-89-4400-54916.

¹³ sarah.meister@med.uni-muenchen.de

¹⁴ laura.hahn@med.uni-muenchen.de

¹⁵ susanne.beyer@med.uni-muenchen.de

¹⁶ corinna.paul@med.uni-muenchen.de

¹⁷ sophie.mitter@med.uni-muenchen.de

¹⁸ Christina.kuhn@uk-augsburg.de

¹⁹ viktoriaschoenfeldt@med.uni-muenchen.de

²⁰ stefanie.corradini@med.uni-muenchen.de

²¹ kritika.sudan@med.uni-muenchen.de

²² christian.schulz@med.uni-muenchen.de

²³ theresa.kolben@med.uni-muenchen.de

²⁴ sven.mahner@med.uni-muenchen.de

²⁵ udo.jeschke@med.uni-muenchen.de

²⁶ thomas.kolben@med.uni-muenchen.de