For immunohistochemical examination of endometrial uNK and plasma cells as well as for micro/molecular biological germ diagnostics a biopsy of the endometrium is required. This procedure can be performed on an outpatient basis by your gynecologist. We recommend to take the sample between the 19th and 22nd day of the cycle, or 5-8 days after ovulation, when the embryo naturally implants in the endometrium.

The preparation of the results and reports usually takes 1 week after receipt of the sample, which are then immediately communicated to your physicians.

Costs according to GOÄ (German scale of fees for physicians)

Initial analysis:
Combined analysis of the number of uterine natural killer cells **AND** plasma cells.. **226.20 €**
Analysis of the number of uterine natural killer cells (CD56+)..... **128.28 €**
Analysis of the number of uterine plasma cells (CD138 marker)..... **128.28 €**

Control analysis:
Combined analysis of the number of uterine natural killer cells **AND** plasma cells.. **128.28 €**
Analysis of the number of uterine natural killer cells (CD56+)..... **79.32 €**
Analysis of the number of uterine plasma cells (CD138 marker)..... **79.32 €**

Additional offers for individual therapy recommendation
Cytotoxic activity of uterine NK cells (CD16+) *
..... **additional 48.96 €**

* analysis of cytotoxic-active CD16+ cells will be carried out only upon analysis of CD56+ uNK cells with levels of 100-400 uNK cells/mm²

Endometrial germ analysis (micro/molecular biological analysis) ** ..... **additional 99.09 €**

** micro/molecular biological analysis for analysis of CD138+ plasma cells, submission of an additional tissue sample in culture medium necessary

Additional costs of 5,95 € may incur for postage and shipping material.

SUMMARY

- **processing of samples only with signed treatment order**
- **sample collection at day 19-22 of a natural cycle or 5-8 days after ovulation**
- **minimum tissue sample size: 3 × 3 × 3 mm for immunhistochemical analysis and 1 x 1 x 1 mm for micro/molecular biological germ analysis**
- **storage and transport in 4-5 % formalin for immunohistochemical staining or in culture medium for micro/molecular biological germ analysis**
- **further information and shipping material available via our web site**

Diagnostic-Team

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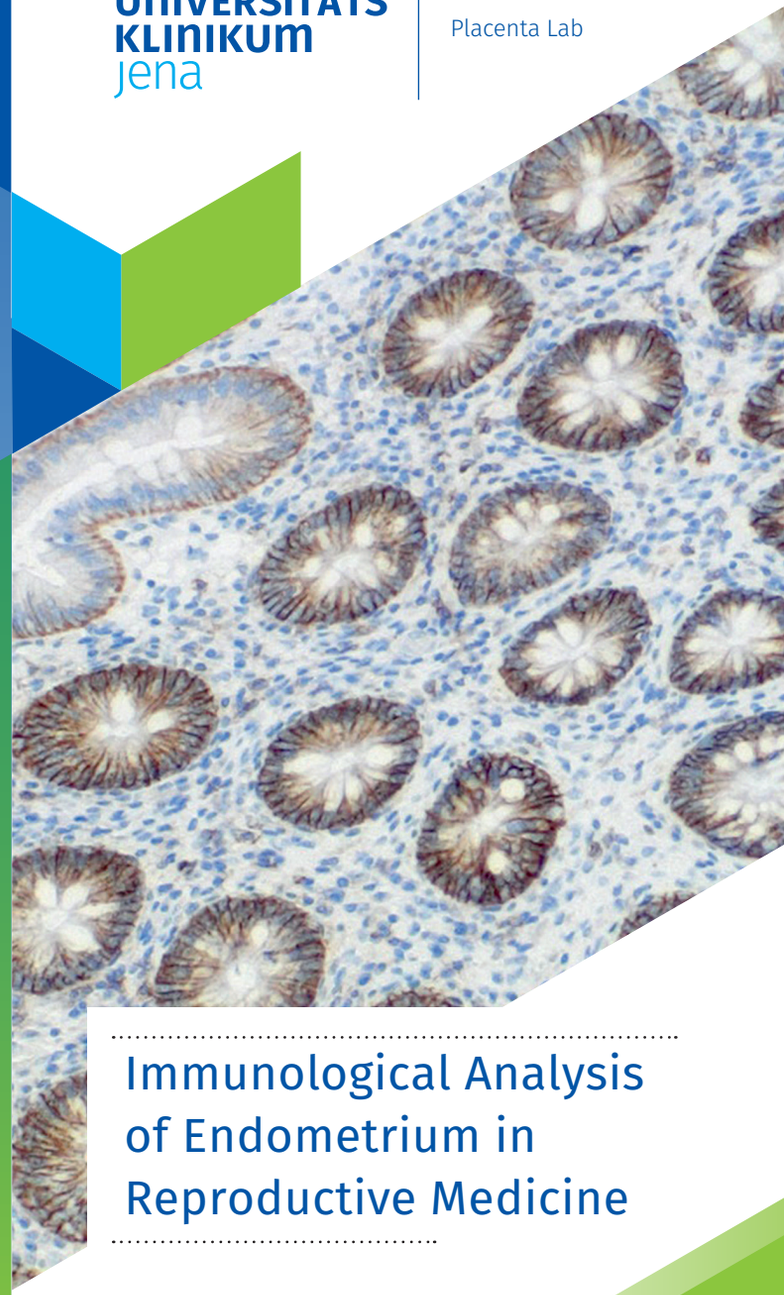
Clinic Director
Department of Obstetrics

Version 2024

UNIVERSITÄTS KLINIKUM Jena | Placenta Lab



Immunological Analysis of Endometrium in Reproductive Medicine

Dear Patient,

Our immune system plays a crucial role not only in everyday life, but also in pregnancy. It plays a decisive role in ensuring successful implantation and to avoid pregnancy complications.

Natural killer cells (NK cells) and plasma cells are important elements of the innate and acquired immunity. The natural function of NK cells is the defense against viruses and the recognition of infected cells. NK cells are present in both blood and endometrium. The NK cells in the endometrium are called uterine NK cells. Plasma cells are activated after contact with a pathogen, produce antibodies, and thus, contribute to the local protection against infection. An elevation of uNK cell numbers and their cytotoxic activity, as well as the presence of plasma cells in the endometrium may disturb the implantation of an embryo and hinder the establishment of a pregnancy.

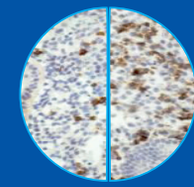
In our placenta laboratory we can detect these immune cells in your endometrial tissue samples by performing a specific immunohistochemical staining. In case the uNK cell numbers are close to the threshold of beeing diagnosed as elevated, we also offer a further investigation of their cytotoxic activity. We thereby hope to support your individual therapy decision. Furthermore, we offer microbiological examinations to detect bacteria in the endometrium, which may cause a chronic endometritis.

We wish you all the best!

Prof. Dr. E. Schleußner

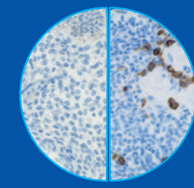
Prof. Dr. U. Markert

Uterine Natural Killer cells (uNK cells, CD56+)



NK cells are among the most important uterine immune cells during early pregnancy. Thus, during the first third of pregnancy, 70% of the placental leukocytes are uNK cells. International studies have described elevated uNK cell counts in the endometrium of women with implantation failure and/or increased miscarriages. It is possible that the accumulation of uNK cells in the endometrium may prevent the implantation of the embryo or lead to a rejection reaction. In case of abnormal results, i.e., > 300 uNK cells/mm² during the potential implantation phase, mild immunoregulatory therapy can be applied to reduce their number and activity.

Plasma cells (CD138+) Chronic endometritis



Chronic endometritis (CE) is usually caused by bacteria. It occurs in about 10-20% of patients with recurrent implantation, idiopathic infertility and repeated miscarriages. However, frequently, the presence of CE is not considered due to the lack of symptoms. CE can be detected by immunohistochemical staining and counting of uterine CD138+ plasma cells. If greater than 4 plasma cells/mm² of endometrial surface, presence of CE may be assumed and can be treated with broad-spectrum antibiotics.

Additional offers for individual therapy recommendation

Cytotoxic activity of uterine NK cells (CD16+)

The cytotoxic activity of uNK cells can be estimated by measuring the surface marker CD16. In case the CD56+ uNK cell numbers are in a range of 100-400 cells/mm² an increased cytotoxic activity, as detectable by an elevated number of CD16+ cells, can contribute to an individual therapy recommendation.

Endometrial germ analysis in chronic endometritis

In the case of persistent CE despite antibiotic therapy, we offer an additional micro/molecular biological analysis in the endometrial tissue. Specific pathogens can be detected and treated.

Therapy control of uNK or plasma cells after previous treatment

To verify the successful treatment of chronic endometritis, we recommend a follow-up biopsy after antibiotic therapy. We also offer a follow-up analysis to check uNK cell numbers after immunoregulatory therapy.