# Uterine Natural Killer Cells

Subjects: Obstetrics & Gynaecology | Reproductive Biology

Contributor: Lenka Lapides, Ivan Varga, Mária Csöbönyeiová, Martin Klein, Lada Pavlíková, Kristína Visnyaiová, Pavel Babál, Renáta Mikušová

Reproductive immunology is at the forefront of research interests, aiming to better understand the mechanisms of immune regulation during gestation. The relationship between the immune system and the implanting embryo is profound because the embryo is semi-allogenic but not targeted by the maternal immune system, as expected in graft-versus-host reactions. The most prominent cell population at the maternal–fetal interface is the population of uterine natural killer (uNK) cells. Uterine NK cells are two-faced immunologically active cells, bearing comparison with Janus, the ancient Roman god of beginnings and endings.

Keywords: uterine NK cells ; endometrium ; histology ; immunohistochemistry ; fertility

## 1. Historical Overview of the Uterine Natural Killer (uNK) Cell's Discovery

The discovery of uNK cells is generally attributed to Herwig Hamperl (1899–1976), one of the most influential and prominent representatives of German pathology in the 20th century [1]. Hamperl is one of the pioneers of fluorescence microscopy, and together with Max Haitinger, they performed the first systematic fluorescence staining in histology [2]. Hamperl (1950), in his first comprehensive work, refers to the newly discovered cells in the endometrium as "fluorescierende Körnchenzellen", which can be translated as fluorescent granular cells or, in shortened form, as "fluorocytes" [3]. In his work, Hamperl mentions that similar cells—argentaffin (take up silver stain) macrophages named "Körnchenzellen"—were described in the inaugural dissertation of W. Dyx in 1941, but the work could not be accessed. In subsequent years, it was discovered that acidophil granulated cells located in the human endometrium and decidua had been observed many years ago by Marchand in 1904 [4] and Weill in 1921 [5], as mentioned by Hellweg in 1959 [6]. Hamperl initially preferred the name "F cells" or fluorocytes, due to the typical fluorescence of these granules in the frozen or paraffin tissue sections when exposed to UV light. They were described as cells 20–30 µm in diameter, with one round-to-oval nucleus and many small granules in the cytoplasm. These granules were described as a little bit larger than granules of eosinophils and usually densely packed in occurrence. In formalin-fixed sections, these cells were without color or were light yellow. They were found in the uterus, endometrial cysts, uterine tubes, breast tissue, cervix, and many locations. Hamperl [3] concluded that the appearance of these cells was typical for tissues with regular bleeding and supposed that these cells were ingesting hemoglobin and other degradation products of cells, using them for their function. In his work in 1954, Hamperl named these cells "endometriale Granulocyten" (i.e., endometrial granulocytes) [7]. Under Professor Hamperl, as the Head of the Institute of Pathology at the University of Bonn in Germany, Gisela Hellweg continued describing these cells in 1956. She called them "Endometrial Körnchenzellen—KZ cells". Hellweg proposed features that distinguished "KZ cells" from neutrophils and eosinophils, such as different morphology of their nuclei and missing positivity for oxidase reactions. She also described their difference with plasma cells because of the atypical nucleus and missing staining affinity for methyl green-pyronin stain or picric acid. In contrast to mast cells, "KZ cells" contained fewer granules and were missing metachromasia, basophilia, and staining with aldehyde fuchsin. According to Hellweg, distinguishing them from lymphocytes was a much more complex issue. Nevertheless, she observed different arrangements of chromatin in the nucleus. Another distinct feature was that "KZ cells" granules lacked affinity to the May–Grünwald–Giemsa stain. Another important observation was the higher occurrence of these cells during the secretory phase of the menstrual cycle. Furthermore, she described that the granules of these cells were filled with protein substances. In contrast to the first description by Professor Hamperl in 1950, she described only those in the uterus [8].

Hamperl and Hellweg (1958) described these cells: "*In the endometrium, during the secretory phase and in the decidua up until three months' gestation, cells appear which contain non-metachromatic granules. These are called granular endometrial stroma cells (Körnchenzellen or K cells). If the presence of K cells is followed during the normal menstrual cycle, it becomes evident that they are absent in the proliferative phase*". The cited authors supposed that they originate from the undifferentiated stromal cell of the endometrium, just like decidual cells. They relied on the observation that they are located in the same places within the pars compacta of the endometrium and around the blood vessels. In addition,

the authors added that "*The K cells were demonstrable in those regions where decidual cell formation had also occurred; that is, in islets of pseudodecidua in the ovary, or under the peritoneum, in a pseudodecidual reaction in the mucosa of the uterine tube with ectopic pregnancy, and endometriosis*" [9].

In the 1980s and early 1990s, after the routine introduction of immunohistochemistry and flow cytometry methods into practice, these uterine cells began to be referred to as "large granular lymphocytes". At the same time, researchers began to investigate the phenotypic similarities and differences between them, peripheral lymphocytes, and NK cells [10][11][12][13][14]. Around 1990, they were finally identified by immunohistochemistry and flow cytometry as a type of natural killer cell with a distinctive phenotype, $CD56^{bright}$, but lacking the other NK cell markers used at the time: CD16 and CD57 [15]. In that time, the first scientific publications that named this cell population as the currently known "uterine/decidual NK cells" were published [16][17][18].

## 2. Terminological Confusions around uNK Cells

There are probably few cells in the human body with as many different names as uNK cells. Eponymously, they are called Hamperl cells after their discoverer [19]. However, according to Winkelmann [20], many anatomical eponyms—including Hamperl cells—are only used by anatomists and have historical value at best. Therefore, they should be dropped from the medical curriculum and everyday clinical practice. Hamperl himself named them "K cells". Surprisingly, this name also appears in contemporary textbooks focused on uterine pathology, such as in [21]. Another historical term, but at the same time an utterly misleading term in the opinion, is "endometrial stromal granulocyte", which nevertheless appears in two contemporary histology textbooks [22][23]. The misleading nature of this term lies in the fact that uNK cells have a different origin, morphology, and function than granulocytes (white blood cells originating from the myeloid lineage). The officially valid and internationally accepted histological nomenclature "Terminologia Histologica" [24] refers to these cells in Latin as "cellula granularis endometrii", with acceptable English equivalents: endometrial granular cells or endometrial natural killer cells (unlike the commonly known term uNK cells). To complicate the matter even further, the world-famous textbook of embryology by Moore et al. [25] uses the terms uNK cells and decidual NK (dNK) cells interchangeably. Moreover, some authors strictly discriminate uNK cells into endometrial NK cells and decidual NK (dNK) cells. Male et al. [26] argued that a specific repertoire of killer immunoglobin-like receptor (KIR) expression which reacts with the fetal HLA-C necessary for trophoblast invasion is found specifically in dNK cells. This makes them distinct from the endometrial NK cells found in the endometrium regardless of pregnancy. A similar strict distinction was discussed by Xie et al. [27], who subdivided uNK cells into non-pregnant endometrial NK cells, which renew over the course of the menstrual cycle. During the menstrual phase, they are discharged with the menstrual blood, becoming "menstrual blood NK cells". On the other hand, dNK cells are pregnancy-associated NK cells which share some phenotypic similarities with endometrial NK cells but are nevertheless different.

## 3. Current Histological Knowledge and Immunohistochemistry of uNK Cells

The uNK cells are sporadically present in the endometrium during the proliferative and early secretory menstrual phases. Their count rises substantially from the mid-secretory phase of the cycle. Their count reaches the maximum in the first trimester. Afterward, their number diminishes. At term of birth, there is only a minimal number of them present. They are also present in the endometrial glands and within the decidua basalis and parietalis, typically surrounding spiral arteries [28]. Studies also indicated that uNK cells are proliferative, especially in the secretory phase of the menstrual cycle, as they were positive for the proliferation marker Ki67 [29].

Morphologically, uNK cells correspond to large granular lymphocytes and belong to innate immunity. They represent 70% of maternal leukocytes during pregnancy. Typical characterization is through phloxinophilic cytoplasmic granules that stain darkly with periodic acid—Schiff staining (PAS reaction), indicating the presence of glycoproteins. These granules usually appear regular, growing in size and number until approximately two weeks of gestation. The granules differ between species in size and content. Human uNK cell granules contain cytotoxic mediators, namely perforin and granzyme. Even though uNK cells are not typically cytotoxic, after exposure to some protein (e.g., interleukin-2), they may become destructive and target extravillous trophoblast [30]. In all species, they have numerous organelles, including mitochondria, a well-developed Golgi apparatus, free ribosomes, and a rough endoplasmic reticulum [31]. The granules of uNK cells are larger compared with granules of peripheral NK cells. NK cells with larger granules are better cytokine producers [32]. Except for granules, uNK cells contain small oval and indented hyperchromatic nuclei [29], and uNK cells produce many cytokines and chemokines like GM-CSF, CSF1, CCL2, CCL3, CCL4, and XCL1 [33]. For the sake of completeness, it is necessary to mention that tissue-specific NK cells are found not only in the uterus but also in various other organs and tissues of the human body (e.g., thymus, spleen, liver, or adipose tissue). All these subpopulations of NK cells may have

differences not only in anatomical location but also in transcription factor requirements, cytokine receptor dependence, and functions [34][35].

Historically, uNK cells were characterized as lymphoid cells that were positive for the common leucocyte antigen (CD45), T-cell antigen CD2 (E-rosette receptor), CD7, CD38 (OKT 10), CD45RO (UCHL1), and MT1-MMP. However, uNK cells are negative for classic natural killer cell markers like Leu 7 and Leu 11 (CD16) [36][37][38][39]. Nowadays, uNK cells are typically defined by their unusual phenotype, which is different from that of peripheral blood cells. Unfortunately, few studies have complexly characterized the phenotype of uNK cells. On the one hand, uNK cells share a similar expression profile of CD56, CD57, CD94, and CD16 with peripheral blood $CD56^{bright}$ NK cells. On the other hand, uNK cells share a similar expression profile of KIR receptors CD158b and NKB1 with $CD56^{dim}$ NK cells, and they also lack the expression of l-selectin. Furthermore, uNK cells were shown to express the activation markers HLA-DR and CD69 [40]. Additionally, it has long been appreciated that uNK cells do not form a uniform population. As in peripheral NK cells, there is cell-to-cell variation in the precise combination of NK cell receptors that are expressed. Recently, however, new single-cell RNA sequencing techniques have enabled an unbiased approach to these cells, and three major subpopulations were identified in first-trimester decidua, originally called dNK1, dNK2, and dNK3 cells [41]. While the function of each subset is unknown, dNK1 cells express transcripts that suggest a role in extravillous trophoblast recognition and interaction; dNK2 cells potentially have anti-inflammatory functions; and dNK3 cells could play a role in extravillous trophoblast regulation. The phenotypes of these different subpopulations of uterine and decidual NK cells were recently reviewed by Male and Moffett [15].

Several research papers used various morphological approaches to study uNK cells, like classic histology, ultrastructural analysis, or immunohistochemistry. Morphological studies elucidated that uNK cells undergo profound changes in the decidua. In mice, uNK cells were observed to form membrane-bound granules, quickly and dramatically increasing in size up to 80 µm [42]. Kusakabe et al. [43] performed a study which examined the morphological changes in uNK cells undergoing cell death during different stages of gestation. The main observations were not surprising, as the uNK cells displayed nucleus condensation, size reduction, and changes in the structure of their granules.

The recent principal histopathological approach in the study of uNK cells in uterine bioptic samples is immunohistochemistry. Most published immunohistochemical studies evaluated the CD56-positive cells in the endometrium and decidua of patients with unexplained recurrent implantation failure and habitual abortion as absolute numbers of CD56-positive cells per square millimeter [44][45][46][47][48][49]. The advantage of such a histological approach is the possibility of studying the cyto-architectonics in the endometrial tissue. Histological specimens allow us to study the mutual spatial relationships between different cells of the endometrium. The disadvantage of the histopathological approach is that uNK cell counting is mostly semi-quantitative, which depends on both the quality and representativeness of the biopsy sample, as well as on the experience of the examining physician (pathologist). The second laboratory approach—which is of significant importance in everyday clinical practice—is the endometrial immune phenotyping of biopsy samples or uterine lavage fluid (and eventually experimentation with menstrual blood) in women with unexplained recurrent implantation failure through flow cytometry [50][51][52][53][54]. More recently, molecular biological approaches (e.g., using single-cell RNA sequencing or mass spectrometry-based proteomics) may also be suitable for making detailed molecular and cellular maps of endometrium in health and disease [55]. These emerging molecular biological technologies hold great promise for providing novel insights into the molecular mechanisms underlying endometrial receptivity and the role of uterine NK cells during successful or unsuccessful embryo implantation [56].

## References


1. Gross, D.; Kaiser, S.; Gräf, C.; Uhlendahl, H.; Schmidt, M. Between fiction and reality: Herwig Hamperl (1899–1976) and the Third Reich as reflected in his autobiography. Pathol. Res. Pract. 2019, 215, 832–841.
2. Haitinger, M.; Hamperl, H. Die Anwendung des Fluoreszenzmikroskops zur Untersuchung tierischer Gewebe. Ztschr. Mikro. Anat. 1933, 33, 193–221.
3. Hamperl, H. Über fluorescierende Körnchenzellen (“Fluorocyten”). Virchows Arch. Pathol. Anat. Physiol. Klin. Med. 1950, 318, 32–47.
4. Marchand, F. On the so-called decidual tumors following normal childbirth, hydatidiform mole and ex-trauterine pregnancy. Obstet. Gynecol. 1895, 1, 419.
5. Weill, P. Etudes sur les leucocytes.I.Les cellules des muqueuses intestinale et uterines. Arch. Anat. Microsc. 1921, 17, 77–82.

6. Hellweg, G. Über körnchenhaltige Zellen im menschlichen und tierischen Endometrium (endometriale Körnchenzellen, metachromasierende Zellen). Z. Zellforsch. Mikrosk. Anat. 1959, 49, 555–568.
7. Hamperl, H. Über endometriale Granulocyten (endometriale Körnchenzellen). Klin. Wochenschr. 1954, 32, 665–668.
8. Hellweg, G. Untersuchungen zur Charakterisierung der Granula in endometrialen Körnchenzellen. Virchows Arch. Pathol. Anat. Physiol. Klin. Med. 1956, 329, 111–120.
9. Hamperl, H.; Hellweg, G. Granular endometrial stroma cells. Obstet. Gynecol. Surv. 1958, 13, 891–893.
10. Bulmer, J.N.; Pace, D.; Ritson, A. Immunoregulatory cells in human decidua: Morphology, immunohistochemistry and function. Reprod. Nutr. Dev. 1988, 28, 1599–1614.
11. Starkey, P.M.; Sargent, I.L.; Redman, C.W. Cell populations in human early pregnancy decidua: Characterization and isolation of large granular lymphocytes by flow cytometry. Immunology 1988, 65, 129–134.
12. King, A.; Wellings, V.; Gardner, L.; Loke, Y.W. Immunocytochemical characterization of the unusual large granular lymphocytes in human endometrium throughout the menstrual cycle. Hum. Immunol. 1989, 24, 195–205.
13. Starkey, P.M.; Clover, L.M.; Rees, M.C. Variation during the menstrual cycle of immune cell populations in human endometrium. Eur. J. Obstet. Gynecol. Reprod. Biol. 1991, 39, 203–207.
14. Bulmer, J.N.; Morrison, L.; Longfellow, M.; Ritson, A.; Pace, D. Granulated lymphocytes in human endometrium: Histochemical and immunohistochemical studies. Hum. Reprod. 1991, 6, 791–798.
15. Male, V.; Moffett, A. Natural Killer Cells in the Human Uterine Mucosa. Annu. Rev. Immunol. 2023, 41, 127–151.
16. Croy, B.A.; Waterfield, A.; Wood, W.; King, G.J. Normal murine and porcine embryos recruit NK cells to the uterus. Cell. Immunol. 1988, 115, 471–480.
17. Parr, E.L.; Parr, M.B.; Zheng, L.M.; Young, J.D. Mouse granulated metrial gland cells originate by local activation of uterine natural killer lymphocytes. Biol. Reprod. 1991, 44, 834–841.
18. King, A.; Balendran, N.; Wooding, P.; Carter, N.P.; Loke, Y.W. CD3− leukocytes present in the human uterus during early placentation: Phenotypic and morphologic characterization of the CD56++ population. Dev. Immunol. 1991, 1, 169–190.
19. Burdan, F.; Dworzański, W.; Cendrowska-Pinkosz, M.; Burdan, M.; Dworzańska, A. Anatomical eponyms—unloved names in medical terminology. Folia Morphol. 2016, 75, 413–438.
20. Winkelmann, A. Should we teach Abernethy and Zuckerkandl? Clin. Anat. 2012, 25, 241–245.
21. Fadare, O.; Roma, A.A. Atlas of Uterine Pathology; Springer Nature: Berlin/Heidelberg, Germany, 2019; p. 269.
22. Young, B.; O'Dowd, G.; Woodford, P. Wheaters's Functional Histology, 6th ed.; Elsevier Churchill Livingstone: Amsterdam, The Netherlands, 2014.
23. Mills, S.E. (Ed.) Histology for Pathologists, 5th ed.; Wolters Kluwer: Tokyo, Japan, 2020.
24. FIPAT. Terminologia Histologica: International Terms for Human Cytology and Histology, 1st ed.; Lippincott Raven: Philadelphia, PA, USA, 2008.
25. Moore, K.L.; Persaud, T.V.N.; Torchia, M.G. The developing human. In Clinically Oriented Embryology, 11th ed.; Elsevier: Amsterdam, The Netherlands, 2020.
26. Male, V.; Sharkey, A.; Masters, L.; Kennedy, P.R.; Farrell, L.E.; Moffett, A. The effect of pregnancy on the uterine NK cell KIR repertoire. Eur. J. Immunol. 2011, 41, 3017–3027.
27. Xie, M.; Li, Y.; Meng, Y.Z.; Xu, P.; Yang, Y.G.; Dong, S.; He, J.; Hu, Z. Uterine Natural Killer Cells: A Rising Star in Human Pregnancy Regulation. Front. Immunol. 2022, 13, 918550.
28. Bulmer, J.N.; Lash, G.E. The Role of Uterine NK Cells in Normal Reproduction and Reproductive Disorders. Adv. Exp. Med. Biol. 2015, 868, 95–126.
29. Pace, D.; Morrison, L.; Bulmer, J.N. Proliferative activity in endometrial stromal granulocytes throughout menstrual cycle and early pregnancy. J. Clin. Pathol. 1989, 42, 35–39.
30. King, A.; Loke, Y.W. Human trophoblast and JEG choriocarcinoma cells are sensitive to lysis by IL-2-stimulated decidual NK cells. Cell. Immunol. 1990, 129, 435–448.
31. Croy, B.A.; Kiso, Y. Granulated metrial gland cells: A natural killer cell subset of the pregnant murine uterus. Microsc. Res. Tech. 1993, 25, 189–200.
32. Goodridge, J.P.; Jacobs, B.; Saetersmoen, M.L.; Clement, D.; Hammer, Q.; Clancy, T.; Skarpen, E.; Brech, A.; Landskron, J.; Grimm, C.; et al. Remodeling of secretory lysosomes during education tunes functional potential in NK cells. Nat. Commun. 2019, 10, 514.

33. Huhn, O.; Ivarsson, M.A.; Gardner, L.; Hollinshead, M.; Stinchcombe, J.C.; Chen, P.; Shreeve, N.; Chazara, O.; Farrell, L.E.; Theorell, J.; et al. Distinctive phenotypes and functions of innate lymphoid cells in human decidua during early pregnancy. Nat. Commun. 2020, 11, 381.

34. Sojka, D.K.; Tian, Z.; Yokoyama, W.M. Tissue-resident natural killer cells and their potential diversity. Semin. Immunol. 2014, 26, 127–131.

35. Haugstøyl, M.E.; Cornillet, M.; Strand, K.; Stiglund, N.; Sun, D.; Lawrence-Archer, L.; Hjellestad, I.D.; Busch, C.; Mellgren, G.; Björkström, N.K.; et al. Phenotypic diversity of human adipose tissue-resident NK cells in obesity. Front. Immunol. 2023, 14, 1130370.

36. Bulmer, J.N.; Sunderland, C.A. Immunohistological characterization of lymphoid cell populations in the early human placental bed. Immunology 1984, 52, 349–357.

37. Bulmer, J.N.; Hollings, D.; Ritson, A. Immunocytochemical evidence that endometrial stromal granulocytes are granulated lymphocytes. J. Pathol. 1987, 153, 281–288.

38. Bulmer, J.N.; Lunny, D.P.; Hagin, S.V. Immunohistochemical characterization of stromal leucocytes in non-pregnant human endometrium. Am. J. Reprod. Immunol. Microbiol. 1988, 17, 83–90.

39. Ritson, A.; Bulmer, J.N. Endometrial granulocytes in human decidua react with a natural-killer (NK) cell marker, NKH1. Immunology 1987, 62, 329–331.

40. Manaster, I.; Mandelboim, O. The unique properties of uterine NK cells. Am. J. Reprod. Immunol. 2010, 63, 434–444.

41. Vento-Tormo, R.; Efremova, M.; Botting, R.A.; Turco, M.Y.; Vento-Tormo, M.; Meyer, K.B.; Park, J.E.; Stephenson, E.; Polański, K.; Goncalves, A.; et al. Single-cell reconstruction of the early maternal-fetal interface in humans. Nature 2018, 563, 347–353.

42. Croy, B.A.; Zhang, J.; Tayade, C.; Colucci, F.; Yadi, H.; Yamada, A.T. Analysis of uterine natural killer cells in mice. Methods Mol. Biol. 2010, 612, 465–503.

43. Kusakabe, K.; Okada, T.; Sasaki, F.; Kiso, Y. Cell death of uterine natural killer cells in murine placenta during placentation and preterm periods. J. Vet. Med. Sci. 1999, 61, 1093–1100.

44. Lapides, L.; Klein, M.; Belušáková, V.; Csöbönyeiová, M.; Varga, I.; Babál, P. Uterine Natural Killer Cells in the Context of Implantation: Immunohistochemical Analysis of Endometrial Samples from Women with Habitual Abortion and Recurrent Implantation Failure. Physiol. Res. 2022, 71, S99–S105.

45. Lapides, L.; Varga, I.; Klein, M.; Rybánska, L.; Belušáková, V.; Babál, P. When Less Is More—Pipelle Endometrial Sampling for Quantification of Uterine Natural Killer Cells in Patients With Recurrent Implantation Failure or Habitual Abortion. Physiol. Res. 2022, 71, S65–S73.

46. Kuon, R.J.; Weber, M.; Heger, J.; Santillán, I.; Vomstein, K.; Bär, C.; Strowitzki, T.; Markert, U.R.; Toth, B. Uterine natural killer cells in patients with idiopathic recurrent miscarriage. Am. J. Reprod. Immunol. 2017, 78, e12721.

47. Alfer, J.; Fattahi, A.; Bleisinger, N.; Antoniadis, S.; Krieg, J.; Dittrich, R.; Beckmann, M.W.; Hartmann, A.; Popovici, R.M.; Tremellen, K. Individual dynamics of uterine natural killer cells in natural and stimulated cycles monitored using a new endometrial dating method. Am. J. Reprod. Immunol. 2022, 88, e13620.

48. Yang, W.J.; Chen, X.; Zhao, Y.; Cheung, W.C.; Hsiao, S.Y.; Liu, Y.; Law, T.S.M.; Chung, J.P.W.; Li, T.C. A comparison of uterine natural killer cell density in the peri-implantation period between natural cycles and hormone replacement therapy cycles. Am. J. Reprod. Immunol. 2019, 82, e13156.

49. Zhao, Y.; Man, G.C.W.; Wang, J.; Liu, Y.; Kwong, J.; Zhang, T.; Chung, J.P.W.; Wang, C.C.; Chen, X.; Li, T.C. The identification of endometrial immune cell densities and clustering analysis in the mid-luteal phase as predictor for pregnancy outcomes after IVF-ET treatment. J. Reprod. Immunol. 2021, 148, 103431.

50. Sudoma, I.; Goncharova, Y.; Dons'koy, B.; Mykytenko, D. Immune phenotype of the endometrium in patients with recurrent implantation failures after the transfer of genetically tested embryos in assisted reproductive technology programs. J. Reprod. Immunol. 2023, 157, 103943.

51. Marron, K.; Harrity, C. Potential utility of a non-invasive menstrual blood immunophenotype analysis in reproductive medicine. Reprod. Fertil. 2022, 3, 255–261.

52. Li, Y.; Yu, S.; Huang, C.; Lian, R.; Chen, C.; Liu, S.; Li, L.; Diao, L.; Markert, U.R.; Zeng, Y. Evaluation of peripheral and uterine immune status of chronic endometritis in patients with recurrent reproductive failure. Fertil. Steril. 2020, 113, 187–196.e1.

53. Marron, K.; Walsh, D.; Harrity, C. Detailed endometrial immune assessment of both normal and adverse reproductive outcome populations. J. Assist. Reprod. Genet. 2019, 36, 199–210.

54. Tohma, Y.A.; Musabak, U.; Gunakan, E.; Akilli, H.; Onalan, G.; Zeyneloglu, H.B. The Role of Analysis of NK Cell Subsets in Peripheral Blood and Uterine Lavage Samples in Evaluation of Patients with Recurrent Implantation Failure. J. Gynecol. Obstet. Hum. Reprod. 2020, 49, 101793.
55. Lai, Z.-Z.; Wang, Y.; Zhou, W.-J.; Liang, Z.; Shi, J.-W.; Yang, H.-L.; Xie, F.; Chen, W.-D.; Zhu, R.; Zhang, C.; et al. Single-cell transcriptome profiling of the human endometrium of patients with recurrent implantation failure. Theranostics 2022, 12, 6527–6547.
56. Bajpai, K.; Acharya, N.; Prasad, R.; Wanjari, M.B. Endometrial Receptivity During the Preimplantation Period: A Narrative Review. Cureus 2023, 15, e37753.