MAKU J. Health Sci. Inst. 2023, 11(3): 293-299.
doi: 10.24998/maeusabed.1334612

Mehmet Akif Ersoy University
Journal of Health Sciences Institute
http://dergipark.gov.tr/maeusabed

Research Article / Araştırma Makalesi

Histological Demostration of Changes in Connective Tissue Components in Uterine Tissue Undergoing Decidualization on Days 4th, 5th and 8th Days of Mause Pregnancy

Fare Gebeliğinin 4., 5. ve 8. Günlerinde Desidualizasyon Geçiren Uterus Dokusunda Bağ Dokusu Elemanlarındaki Histolojik Değişimin Gösterilmesi

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Abstract: This study examined the changes in connective tissue elements of the uterine undergoing decidualization on the 4th, 5th, and 8th days of pregnancy by histochemical methods. Forty Balb/c 6-8 weeks-old female mice divided into four groups as non-pregnant estrous phase, 4th, 5th, and 8th-day pregnancy models. Five µm thick sections were taken from paraffin blocks obtained from uterine tissues. Samples were stained with Hematoxylin&Eosin, Mallory Azan, Orsein, and Periodic Acid Schiff stains. As a result of the staining, the uterine tissue in the non-pregnant estrus phase showed standard histological structure. On the 4th day of pregnancy, the amount of intensely stained collagen and elastic fiber decreased on the 5th day of gestation; On the 8th day of pregnancy, it was determined that the density of the fibers increased again. As a result, both increased collagen and elastic fibers for its placement to an elastic-solid uterine tissue and increased carbohydrates for its nutrient needs and immune privilege were demonstrated in the uterus for the 4th-day embryo. The decrease in connective tissue elements with the acceleration of decidualization on the 5th and increased collagen and elastic fibers in the myometrium and the PAS + NK cells in the endometrium on the 8th-day was noted.

Keywords: Connective tissue, Decidualization, Histochemistry, Pregnancy.

Öz: Bu çalışmada, fare gebeliğinin 4., 5. ve 8. günlerinde desidualizasyon geçiren uterus dokusunun bağ dokusu elemanlarındaki değişim histokimyasal yöntemlerle incelendi. Çalışmada, 40 adet 6-8 haftalık Balb/c ırkı fareler, gebe olmayan östrus fazı, 4., 5. ve 8. gün gebelik modelleri şeklinde dört gruba ayrıldı. Uterustan elde edilen parafin bloklardan 5 µm kalınlığında kesitler alındı. Örnekler, Hematoksilen&Eosin, Mallory Azan, Orsein ve Periyodik Asit Schiff boyaları ile boyandı. Boyamalar sonucunda gebe olmayan östrus fazındaki uterus dokusunda standart histolojik yapı izlendi. Gebeliğin 4. gününde yoğun boyanan kollajen ve elastik lif miktarının gebeliğin 5. gününde azaldığı; gebeliğin 8. gününde ise liflerin yoğunluğunun tekrar arttığı belirlendi. Sonuç olarak, 4 günlük embriyonun uterus içerisine yerleşmesi ve ihtiyaçlarına rahat ulaşması için elastikiyete sahip sağlam bir uterus dokusu oluşumu kolajen ve elastik liflerin artışı da, beslenmesi için gerekli olan karbonhidrat artışı da PAS reaksiyonu ile gösterildi. 5. günde desidualizasyonun da hız kazanmasıyla bağ dokusu elemanlarındaki azalma, 8 günde ise embriyonunda büyümeye başlamasıyla miyometriumda kollajen ve elastik lif miktarının, endometriumda ise PAS+ NK hücrelerinin artışı dikkat çekti.

Anahtar Kelimeler: Bağ doku, Desidualizasyon, Histokimya, Gebelik.

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Geliş tarihi / Received : 04.08.2023
Kabul tarihi / Accepted: 12.10.2023

Introduction

Successful pregnancy depends on a healthy uterus suitable to receive and support a fertilized embryo and the process of decidualization. The stromal cells surrounding the embryo also change during gestation, a process crucial for implantation known as decidualization. The uterus is an essential organ that undergoes morphological and physiological changes during pregnancy to support the development of the embryo and fetus. The

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ISSN: 2148-2837/ MAKU J. Health Sci. Inst.

uterine wall has three layers: the endometrium, myometrium, and perimetrium (Mescher, 2018). The endometrial mucosa is a thick layer of connective tissue containing numerous glands, fibroblasts, and abundant extracellular substances. The myometrium surrounds the endometrium and undergoes growth during pregnancy through the enlargement of smooth muscles (hypertrophy) and increased muscle fibers (hyperplasia). The myometrium contains collagen and elastic fibers, especially in the loose connective tissue between the muscle bundles, to strengthen the uterus during pregnancy. Fibroblasts, histiocytes, macrophages, and mast cells are also present (Kierszenbaum and Tres, 2021).

In mice, decidualization, the process of stromal cell transformation in the uterus, occurs after the blastocyst attaches to the uterine epithelium (Wang et al., 2020). Decidualization occurs in the anti-mesometrial side of the uterus, where implantation takes place (Croy et al., 2014). The connective tissue stromal cells change, and decidual cells form the decidua uterine mucosa called (Ramathal et al., 2010). Decidua formation in mice begins around the 4.5-5th day of pregnancy following implantation (Das, 2010; Ramathal et al., 2010). It has been reported in the literature that changes in the number and distribution of many cells and fibers in the uterine tissue in the preparation of the endometrium for embryo implantation, and development has been reported in the literature (Teodoro et al, 2003; Stumm and Zorn, 2007).

The aim of this study is to investigate the changes in the connective tissue elements of the uterine tissue undergoing decidualization on the 4th, 5th, and 8th days of pregnancy by histochemical methods and to contribute to the literature on this subject.

Materials and Methods

The Akdeniz University Animal Experiments Local Ethics Committee approved the experimental protocol with protocol number 2022.01.007. In the study, 40 Balb/c female mice, of about 6-8 weeks old and weighing 20±25 g. were provided from the Akdeniz University Experimental Animals Research and Application Center. Each mouse was kept in standard laboratory conditions with a 12-hour dark/light cycle at 21±2 °C room temperature.

The mice were randomly divided into four groups were established, with 10 animals in each group representing the non-pregnant estrus phase (EP) and days 4 (P4), 5 (P5), and 8 (P8) of pregnancy. While forming the groups, vaginal smears were made to determine the estrus phase of non-pregnant female mice and stained with toluidine blue. Mice with a squamous (crustaceous) structure and a predominance of large, non-nucleated epithelial cells were included in the experiment. Two female mice were left in the same cage with a male mouse to mate, and pregnancy was detected by vaginal plate. Females with a vaginal plaque were accepted on the 1st day of pregnancy. To determine whether females on the 4th day of pregnancy are pregnant, one of the uterine horns was washed with PBS, and the tubal fluid obtained after washing was examined under the microscope, and the presence of blastocyst was determined. Tissue samples were taken from the other uterine horn not washed for the blastocyst. To determine whether the females were pregnant on the 5th day of pregnancy, females were sacrificed 3-4 minutes after the tail vein injection of Chicago Blue. Mice whose implantation sites were observed as blue bands were confirmed to be pregnant. On the 8th day of pregnancy, the implantation sites can be seen with the naked eye. Females with implantation sites were included in the experiment. The mice were anesthetized with ketamine (100 mg/kg; Alfasan) + xylazine hydrochloride (10 mg/kg; Bayer). Mice were sacrificed by cervical dislocation, and uterine tissue samples were collected and fixed in a 10% formaldehyde solution. Paraffin blocks were prepared from these tissues, and sections with a thickness of 5 μm were obtained. The sections were deparaffinized and rehydrated. The samples' histopathology was evaluated via Hematoxylin&Eosin (H&E) staining and also preferred to stain with Mallory's Azan (MA) for collagen fibers, Orcein for elastic fibers, and

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Periodic Acid Schiff (PAS) to show glycogen content in uterine decidua cells.. The slides were examined using an axioplan microscope (Zeiss, Germany) and photographed.

Results

The examinations performed on tissue sections stained with Mallory Azan, Orsein, and PAS stain in the non-pregnant estrus phase and on the 4th, 5th, and 8th days of pregnancy are shown in Figure 1. The connective tissue of the endometrial layer for EP appeared normal, and the collagen fiber arrangement in the uterus's surface and deep layers showed a regular course. However, the density of elastic fibers in the uterine tissue was low, as observed in the preparations stained with Orcein. The PAS reaction indicated a normal appearance of the basement membrane, uterus, and glandular epithelial surface in the uterine tissue (Figure 1.EP). On the 4th day of pregnancy (Figure 1.P4), notable changes were observed in the uterine tissue. Decidualization, the process of preparing the endometrium for implantation, was spreading toward the anti-mesometrial side. The endometrial stroma exhibited a looser structure in this region, and the uterine glands were predominantly located near the myometrium rather than in the decidual area. Collagen fibers were present between the endometrial stromal cells and around the glands, as well as in the connective tissue between the smooth muscles of the myometrium. Elastic fibers were observed on the surface parts of the uterine epithelium. PAS positivity was observed on the surface of the uterine luminal epithelium, basement membrane, and glandular epithelial cells, indicating the presence of glycogen in the uterine decidua cells.

Further changes were evident in the uterine tissue by the 5th day of pregnancy (Figure 1.P5). Blood vessels originating from secondary decidual cells were observed in the decidual area, indicating increased vascularization. The maternal blood vessels dilated, and the glands in the endometrial stroma became scattered and more minor. Decidualization occurred predominantly in the anti-mesometrial area, leading to the emergence of the primary decidual region. Collagen fibers became sparse in the endometrial stroma, and their density decreased in the connective tissue between the smooth muscles of the myometrium. Weak staining of elastic fibers was observed between the longitudinal muscle bundles of the myometrium. Elastic fibers arranged in black strands were also observed around the luminal epithelium. PAS positivity was observed on the surface of the uterine luminal epithelium, basement membrane, surface of glandular epithelial cells, and vessel walls, indicating the presence of glycogen.

On the 8th day of pregnancy (Figure 1.P8), as the primary decidual zone regressed and the secondary decidual zone emerged, more intense collagen fibers were observed around the decidual cells in the endometrium. Elastic fibers were observed between the longitudinal muscle bundles of the myometrium, and positive staining was detected on the surface of blood vessels. PAS positivity was observed on the surface of the uterine luminal epithelium, basement membrane, surface of glandular epithelial cells, and vessel walls. Additionally, a granular PAS reaction was strongly detected in decidual cells, and the cells thought to be uterine natural killer (uNK) cells were also observed.

These observations provide insights into the dynamic changes that occur in the uterine tissues during different stages of pregnancy, highlighting alterations in the histological structure, distribution of collagen and elastic fibers, and the presence of glycogen in uterine decidua cells.

Discussion

The development of the embryo to the blastocyst stage, implantation into the uterine endometrium, and forming a functional placenta are crucial for establishing a pregnancy. The success of implantation ultimately depends on ensuring proper trophoblast growth and regulating invasion into the endometrium to establish a blood supply for the conceptus (Dimitriadis et al., 2005).

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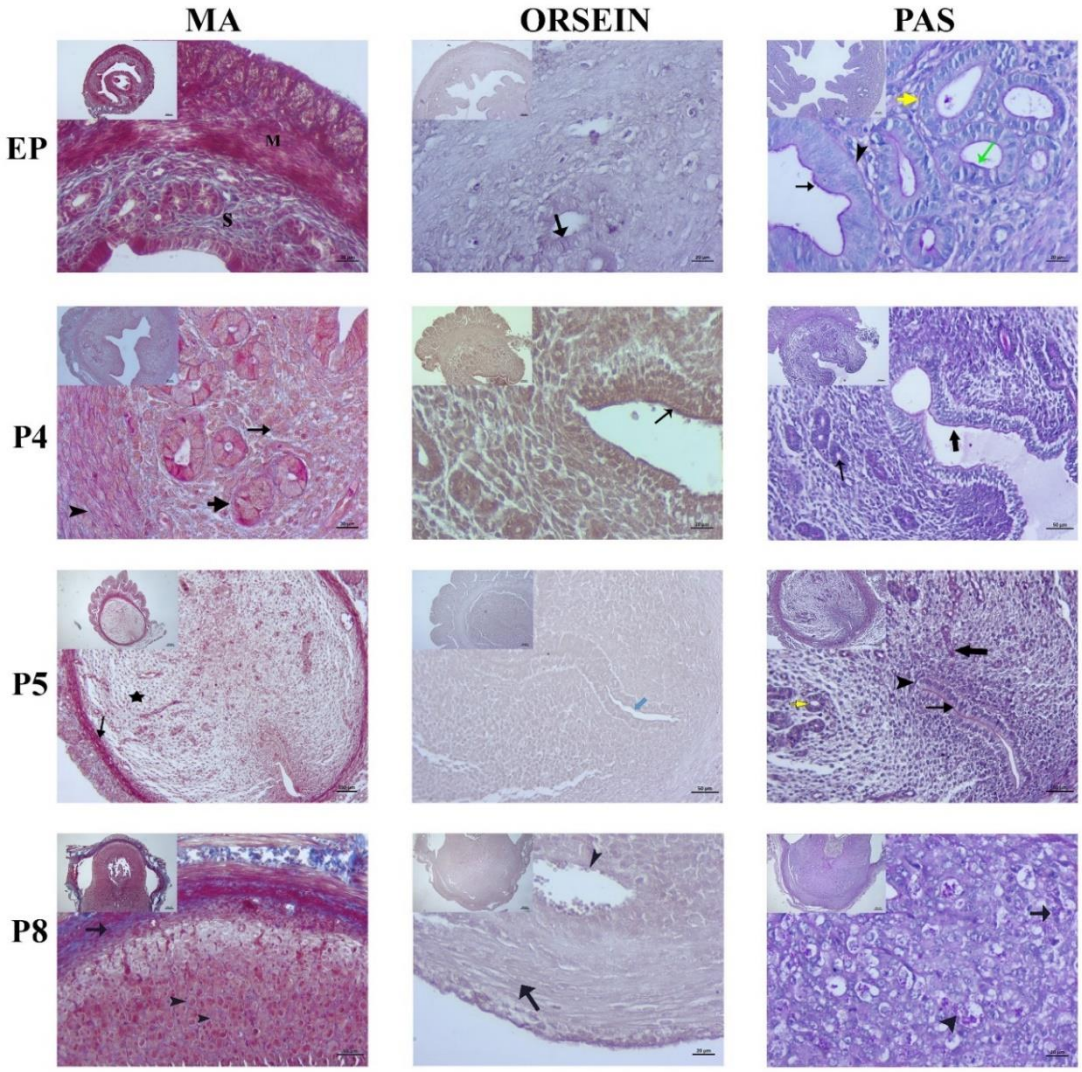

Figure 1. Light microscopic images of mouse non-pregnant estrus phase and uterine tissue from the 4th, 5th, and 8th day of pregnancy. Regular distribution of collagen fibers in the connective tissue of the endometrial stroma (S) and myometrium (M) in the non-pregnant estrus phase (EP) mouse uterus. In the P4, collagen fibers were seen between stromal cells of the uterine endometrium (thin arrow), around the uterine glands (thick arrow), and in the connective tissue between smooth muscles of the myometrium (arrowhead). In the P5, Decreased density of collagen fibers (asterisk), which are scattered and sparse in the endometrial stroma, in the connective tissue between the smooth muscles of the myometrium (arrow). In the P8, dense collagen fibers in the myometrium (arrow), collagen fibers around decidual cells in the endometrium (arrowheads). MA staining method. Bar: 20-100 μm. The density of elastic fibers in the surface parts of the uterine epithelium (arrow) in the P4 and uterine gland (arrow) in the EP. Reduced density of elastic fibers on the surface of the uterine epithelium (blue arrow) in the P5. Increased density of elastic fibers between the muscle bundles of the myometrium (arrow). Also, prominent elastic fiber structure on the surface of the blood vessels (arrowheads) in the P8. Orcein Staining method. Bar: 20-100 μm. Normal appearance of the basement membrane (yellow arrow), uterus (thin arrow and arrowhead), and glandular epithelial surface (green arrow) in the uterine tissue in the EP. PAS positivity on the surface parts of the uterine epithelium (thick arrow) and the surface of uterine gland epithelial cells (thin arrow) in the P4. PAS staining method. PAS reaction with decreased intensity on the surface of the uterine epithelium (arrow) and basement membrane (arrowhead) and PAS reaction on the surface of the uterine gland epithelial cells (yellow arrow) and vessel walls in the uterus (thick arrow) in the P5. Strong PAS reaction in granular form in uterine decidua cells (arrowhead) and uNK cells (arrow) in the P8. PAS staining method. Bar: 20-100 μm.

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This study was planned to investigate histochemical changes in connective tissue elements in the non-pregnant estrous phase of mouse and uterine tissue undergoing decidualization on days 4, 5, and 8 of gestation at the light microscopic level.

Decidualization is the most important determinant of pregnancy success. Decidual stromal cells help vascular adaptation, suppress inflammation, provide tolerance to fetal antigens, and are genetically reprogrammed versions of endometrial stromal cells. Unlike many mammals, decidualization tissue is formed in humans every menstrual cycle. In other species, this can occur in the presence of a blastocyst (Ng et al., 2020).

Electron microscopic examination of the uterus of pregnant mice (Abrahamsohn, 1983) showed that on day 5 of gestation, decidual cells with round nuclei and free ribosomes predominated in the cytoplasm; on days 6 to 8, the cytoplasm of these cells contained numerous granular and agranular endoplasmic reticulum, microfilament bundles, and lipid droplets in addition to well-developed Golgi complexes, mitochondria, and lysosomes. Another study reported that collagen fibers of approximately 40 nm in size in non-pregnant mouse uterine endometrium were transformed by decidual cells into fibrils larger than 400 nm showing irregular profiles (Croy et al., 2014). Spiess et al.(2007?) argued that collagen types I, III, and V are the main components of non-pregnant and pregnant mouse endometrium. When they looked at the immunolocalization of Collagen types I, III, and V, they found that it differed between implantation and inter-implantation sites in the mouse uterus during early pregnancy; Collagen type I was widely distributed in the non-decidualized endometrial stroma of the inter-implantation sites; Collagen type V was weakly expressed in the non-decidualized stroma throughout all periods but was more abundant in the decidualized areas on day 7 of pregnancy. Day ? of pregnancy, but was expressed in more significant amounts in decidualized regions (Spiess et al., 2007). In addition, the same researchers also determined that Collagen type V is associated with tiny blood vessels in the endometrium. This study determined that the density of collagen and elastic fibers stained on the 4th day of pregnancy, and decreased on the 5th day of pregnancy. The density of these fibers increased on the 8th day of pregnancy.

Various components of the endometrial extracellular matrix, especially collagen fibrils, undergo morphological and biochemical changes during rodent decidualization (Alberto-Rincon et al., 1989). In a study, it was reported by light and electron microscopic studies that collagen concentration increased in the endometrium of mice on the 7th and 8th days of pregnancy, and collagen fibrils accumulated around the decidual cells (Teodoro et al, 2003). In In this study, it was found an increase in collagen density, especially in the myometrium on the 8th day of gestation, in parallel with the mentioned information. The remodeling of ESM in the early stages of pregnancy in mice was investigated by Croy et al.,(2014) argued that collagen-containing acid phosphatase-positive granules were found in endometrial fibroblasts, suggesting that intracellular degradation of collagen occurs. The same researchers showed the presence of several collagen fibers in the endometrial stroma during the preimplantation period by analysis with transmission electron microscopy. Mutluay (2015) reported that the uterine endometrial connective tissue had a typical structure on day 0, the collagen fiber structure showed a regular course in the surface and a deep endometrial layer of the uterus, and on the 1st day of pregnancy, collagen fibers spread towards the myometrium from the bottom of the decidual area where there was cellular concentration. In this study, the endometrial connective tissue of the non-pregnant mouse uterus in the estrus phase had a standard structure, and the collagen fiber structure in the surface and deep endometrial layer of the uterus showed a regular course.

In a study with fibrillin-1, a glycoprotein involved in the formation of elastic fibers, it was reported that it was found between endometrial fibroblasts and decidual cells in mice before and after implantation, respectively, and that the organization of fibrillin-1 and its distribution in

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various regions of the endometrial stroma depended on the stage of pregnancy (Stumm and Zorn, 2007). In the same study, histochemical staining of elastic fibers revealed that elastic fibers were almost absent in the endometrial stroma during pregnancy. In contrast to this study, elastic fibers arranged in black strands were found around the endometrial luminal epithelium on days 4 and 5 of mouse pregnancy. In addition, on the 8th day of gestation, it was determined that elastic fibers were weakly stained between the myometrium muscle bundles.

In a study conducted on the rat, it was reported by PAS staining that the basement membrane structure in the uterine tissue had a regular appearance on all gestational days and continued uninterruptedly under the epithelial cells (Mutluay, 2015). In another study, PAS positivity was reported in the basement membrane on the fourth day of pregnancy in mice (Koç, 2019). In parallel with these studies, PAS positivity was found in uterine tissue during the non-pregnant estrus phase and pregnancy days.

Studies have shown that the glycoconjugate content in the cytoplasmic granules of uterine Natural Killer (uNK) cells reacts with the periodic acid Shiff's reagent (Stewart and Peel, 1980; Sur et al., 2015). Sur et al. reported that uNK cells showing intense PAS positivity were found in the decidua basalis in mice in the middle and last days of pregnancy (Sur et al., 2015). The number of these cells was reported to be very high in the middle of pregnancy, and a significant decrease was observed towards the end of pregnancy. In another study investigating the 4th, 10th, and 17th days of pregnant mice, it was reported that the cells thought to be PAS-positive uNK reached the highest amount on the tenth gestation day (Koç, 2019). In this study, cells thought to be PAS + granulated uNK were found in the uterine endometrium on day 8 of mouse pregnancy.

In conclusion, it was determined that the connective tissue content of the mouse uterus in the non-pregnant estrus phase and the mouse uterus on the 4th, 5th, and 8th days of pregnancy underwent different structural changes using by histochemical methods. The endometrial connective tissue in the non-pregnant mouse uterus in the estrus phase was observed to have a standard structure. On the 4th day of pregnancy, decidualization was observed to spread toward the anti-mesometrial side of the uterine tissue, where implantation would occur. On the 5th day of gestation, vascularization increased in the decidual area, maternal blood vessels dilated, and the glands in the endometrial stroma were scattered and considerably smaller. It was observed that decidualization occurred in the anti-mesometrial area, and the primary decidual zone appeared. On the 8th day of pregnancy, when the primary decidual zone regressed and the secondary decidual zone emerged, collagen tissue, denser in the myometrium, was observed around the decidual cells in the endometrium. At the same time, more dense elastic fibers were also observed in the myometrium. These data support other studies showing ESM remodeling in mouse endometrial stroma at the onset of pregnancy.

Source(s) of Funding:

This article was supported within the scope of TUBITAK 2209-A University Students Research Projects Support Program 2021, 2 semesters by application 1919B012104121.

Conflict(s) of Interest/ Disclosure(s):

The authors declare no conflict of interest.

References

Abrahamsohn, P.A., 1983. Ultrastructural study of the mouse antimesometrial decidua. Anatomy and Embryology 166(2), 263-274.

Alberto-Rincon, M.C., Zorn, T.M., Abrahamsohn, P.A., 1989. Diameter increase of collagen fibrils of the mouse endometrium during decidualization. The American Journal of Anatomy 186(4), 417-429.

Croy, A., Yamada, A.T., DeMayo, F.J., Adamson, S.L., 2014. The Guide Investigation of Mouse Pregnancy. Elsevier, pp. 1-19.

Das, S.K., 2010. Regional development of uterine decidualization: molecular signaling by Hoxa-10. Molecular Reproduction& Development 77, 387-396.

Dimitriadis, E., White, C.A., Jones, R.L., et al. 2005. Cytokines, chemokines and growth factors in endometrium related to implantation. Human Reproductive Update 11(6), 613-630.

Kierszenbaum, A.L., Tres, L.L., 2021. Histology and Cell Biology An Introduction to Pathology.4th ed. New York, NY, Elsevier.

Koç, S., 2019. Gebeliğin Farklı Dönemlerindeki Fare Plasentasında Histolojik Ve Histokimyasal Değişiklikler İle Igg Dağılımının ve Yoğunluğunun Araştırılması. Histology And Embriyology (Veterinary) Program. Instutie Of Health Sciences: Aydın Adnan Menderes University Aydın.

Mescher, A.L., 2018. Junqueira's Basic Histology Text&Atlas. 15th ed. US: Mc Graw Hill Education.

Mutluay, D., 2015. Examination in the light microscopical level of the changes occurring in the rat uterus tissue during preimplantation. MAKÜ Saglık Bilimleri Enstitütü Dergisi 3(2), 43-53.

Ng, S.W., Norwitz, G.A., Pavlicev, M., et al. 2020. Endometrial Decidualization: The Primary Driver of Pregnancy Health. International Journal of Moleculaar Sciences 21(11).

Ramathal, C.Y., Bagchi, I.C., Taylor, R.N., et al. 2010. Endometrial decidualization: of mice and men. Seminars in Reproductive Medicine 28(1), 17-26.

Spiess, K., Teodoro, W.R., Zorn, T.M. 2007. Distribution of collagen types I, III, and V in pregnant mouse endometrium. Connective Tissue Research 48(2), 99-108.

Stumm, C.L., Zorn, T.M., 2007. Changes in fibrillin-1 in the endometrium during the early stages of pregnancy in mice. Cells Tissues Organs 185, 258-268.

Stewart, I., Peel, S., 1980. Granulated metrial gland cells at implantation sites of the pregnant mouse uterus. Anatomy and Embryology 160(2), 227-238.

Sur, E., Öznurlu, Y., Özaydin, T., Çelik, İ., Aydin, İ., Kadiralieva, N., 2015. Gebe farelerde desidua bazalis dokusundaki pas-pozitif uterus doğal katil hücrelerinin dağılımı. Kafkas Universitesi Veteriner Fakültesi Dergisi 21(3), 4005-4011.

Teodoro, W.R., Witzel, S.S., Velosa, A.P., et al. 2003. Increase of interstitial collagen in the mouse endometrium during decidualization. Connective Tissue Research 44(2), 96-103.

Wang, C., Zhao, M., Zhang, W.Q., et al. 2020. Comparative analysis of mouse decidualization models at the molecular level. Genes 11, 1-12.

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