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ABSTRACT

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IMMUNOHISTOCHEMICAL FEATURES OF BAX-DEPENDENT APOPTOSIS IN THE TROPHOBLAST OF PLACENTAL CHOROIDAL VILLI AT DELIVERY AFTER 40 WEEKS

The relevance of studying the molecular mechanisms that regulate apoptosis in placental tissues, especially in the later stages of pregnancy, is significant for understanding this organ's normal and pathological functioning. Apoptosis, or programmed cell death, is essential for maintaining tissue homeostasis, ensuring normal placental function, and maintaining adequate metabolism between mother and fetus. One of the main proteins that regulate apoptosis is BAX – a molecule that is actively involved in the initiation of this process through the activation of caspases.

The study aimed to determine the features of BAX-dependent apoptosis in the trophoblast of the placental chorionic villi by immunohistochemical method at delivery after 40 weeks.

Materials and methods: The placental material (pieces from the intermediate zone from the fetal plate to the basal plate) was fixed for 22–24 hours in a neutral buffered (Lilly) 10% aqueous formalin solution. Then, the fixed placental material was dehydrated in an ascending alcohol series (from 50 degrees to “absolute” alcohol) and embedded in paraffin at 58 °C.

Histological serial sections of 5 μm thickness were obtained on a sledge microtome MS-2. After deparaffinization of the histological sections, hematoxylin and eosin staining was performed, and immunohistochemical techniques were used on other serial sections in accordance with the manufacturer’s protocols (DAKO). In particular, immunohistochemical reactions with primary antibodies against the pro-apoptotic BAX protein and the anti-apoptotic protein Bcl-2 were performed. Visualization of primary antibodies was carried out using a polymeric system to visualize reaction results with diaminobenzidine dye (it gives a clear brown color to the locations of the studied antigens).

Along with the descriptive method of histopathological examination, we also performed computer morphometry on previously obtained digital

copies of optical microscopic tissue images (Delta Optical Evolution 100 microscope – planachromatic objectives in accordance with the required optical magnification – and Olympus SP550UZ digital camera with an adapter).

Digital copies of the image were analyzed using a legal copy of the ImageJ v1.53t computer program, specialized for digital histometric studies. In particular, the hematoxylin and eosin-stained sections were subjected to a scoring test (repeated counting, which provides data on the proportion of villi with "syncytial nodules").

The digital copies of images with immunohistochemical staining were assessed for specific staining intensity by computerized microdensitometry. To do this, we used the built-in standard tools of the ImageJ v1.53t computer program to obtain the computerized value of color brightness in an 8-bit color analysis system (with a gradation from zero to 255) using the microprobe method. Further, this value was converted to relative optical density (in optical density units) by logarithmic transformation. The value obtained in this way was convenient for interpreting the intensity of color as it ranged from zero (absolute transparency) to one (absolute opacity).

The obtained digital data were processed using statistical methods. In particular, with the help of a legal copy of the computer program for statistical calculations PAST v 4.17, a preliminary test for the normality of the distribution was performed using the Shapiro–Wilk test. According to this criterion, the hypothesis of normality of distribution was not rejected (at p=0.05) for all the studied statistical samples; thus, parametric statistical analysis methods were used: calculation of the arithmetic mean and its error, unpaired two-sided Student's test. In addition to the Student's test, the non-parametric Mann–Whitney test was also used, but statistical significance was reported only for the Student's test.

Results: Thus, from the point of view of molecular regulation of apoptosis in the trophoblast of the placental chorionic villi at delivery after 40 weeks vs. physiological pregnancy and delivery, conditions are created for enhanced trophoblast death by BAX-dependent apoptosis, since there is an increase in the concentration of the pro-apoptotic BAX-protein, while the concentration of its main antagonist, Bcl-2, decreases markedly.

Conclusions: At delivery after 40 weeks, the molecular processes of BAX-dependent apoptosis are activated in the placental trophoblast, and the proportion of villi with syncytial nodules increases accordingly.

Keywords: BAX-dependent apoptosis, trophoblast, chorionic villi, placenta, labor after 40 weeks, pregnancy.

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РЕЗЮМЕ

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ІМУНОГІСТОХІМІЧНІ ОСОБЛИВОСТІ BAX-ЗАЛЕЖНОГО АПОПТОЗУ В ТРОФОБЛАСТІ ХОРІАЛЬНИХ ВОРСИНОК ПЛАЦЕНТИ ПРИ ПОЛОГАХ ПІСЛЯ 40 ТИЖНІВ

Вивчення молекулярних механізмів, що регулюють апоптоз у тканинах плаценти, особливо на пізніх стадіях вагітності, є надзвичайно важливим для розуміння нормального та патологічного функціонування цього органу. Апоптоз, або запрограмована загибель клітин, є важливим процесом для

підтримки гомеостазу тканин, забезпечення нормальної функції плаценти та підтримання адекватного метаболізму між матір'ю та плодом. Одним з основних білків, що регулюють апоптоз, є BAX-молекула, яка бере активну участь в ініціації цього процесу через активацію каспаз.

Мета дослідження – імуногістохімічним методом визначити особливості BAX-залежного апоптозу в трофобласті ворсин хоріона плаценти при розродженні після 40 тижнів.

Матеріали та методи: Плацентарний матеріал (шматочки з проміжної зони від плодової до базальної пластинки) фіксували протягом 22–24 годин у нейтральному забуференому (Lilly) 10% водному розчині формаліну. Потім фіксований плацентарний матеріал зневоднювали у висхідній батареї етанолу (від 50 градусів до «абсолютного» спирту) і заливали в парафін при 58 °С.

Гістологічні серійні зрізи товщиною 5 мкм отримували на санному мікротомі МС-2. Після депарафінізації гістологічних зрізів проводили забарвлення гематоксиліном та еозином, а на інших серійних зрізах використовували імуногістохімічні методи відповідно до протоколів, наданих виробником (DAKO). Зокрема, проводили імуногістохімічні реакції з первинними антитілами проти проапоптичного BAX білка та антиапоптичного білка Bcl-2. Візуалізацію первинних антитіл проводили за допомогою полімерної системи для візуалізації результатів реакції з діамінобензидиновим барвником (надає чітке коричневе забарвлення місцям розташування досліджуваних антигенів).

Крім описового методу гістопатологічного дослідження, проводили також комп'ютерну морфометрію на попередньо отриманих цифрових копіях оптичних мікроскопічних зображень тканин (мікроскоп Delta Optical Evolution 100 – планахроматичні об'єктиви відповідно до необхідного оптичного збільшення – та цифрова камера Olympus SP550UZ з адаптером).

Цифрові копії зображення аналізували за допомогою легальної копії комп'ютерної програми ImageJ v1.53t, спеціалізованої для цифрових гістометричних досліджень. Зокрема, забарвлені гематоксиліном та еозином зрізи піддавали скоринг-тесту (повторний підрахунок, який надає дані про частку ворсинок з «синцитіальними вузликами»).

На цифрових копіях зображень з імуногістохімічним забарвленням оцінювали інтенсивність специфічного забарвлення методом комп'ютерної мікроденситометрії. Для цього вбудованими стандартними засобами комп'ютерної програми ImageJ v1.53t спочатку отримували комп'ютерне значення яскравості кольору в 8-бітній системі аналізу кольору (з градацією від нуля до 255) методом мікрозонда, а потім це значення переводили у відносну оптичну щільність (в одиницях оптичної щільності) шляхом логарифмічного перетворення. Отримане таким чином значення є зручним для інтерпретації інтенсивності кольору, оскільки воно коливається від нуля (абсолютна прозорість) до одиниці (абсолютна непрозорість).

Отримані цифрові дані були оброблені за допомогою статистичних методів. Зокрема, за допомогою легальної копії комп'ютерної програми для статистичних розрахунків PAST v 4.17 було застосовано попередню перевірку на нормальність розподілу за критерієм Шапіро–Уілка. Для всіх досліджуваних статистичних

вибірок за цим критерієм гіпотеза про нормальність розподілу не була відхилена (при p = 0,05), тому були використані параметричні методи статистичного аналізу: обчислення середньої арифметичної та її похибки, непарний двосторонній критерій Ст'юдента. Поряд з критерієм Ст'юдента використовувався також непараметричний критерій Манна–Уітні, але значення вірогідності повідомлялося тільки за критерієм Ст'юдента.

Результати: Таким чином, з точки зору молекулярної регуляції апоптозу в трофобласті ворсин хоріона плаценти при розродженні після 40 тижнів порівняно з фізіологічною вагітністю та пологами створюються умови для посиленої загибелі трофобласта шляхом BAX-залежного апоптозу, оскільки відбувається підвищення концентрації проапоптичного білка BAX, тоді як концентрація його основного антагоніста Bcl-2 помітно знижується.

Висновки: При розродженні після 40 тижнів у трофобласті плаценти активуються молекулярні процеси BAX-залежного апоптозу, відповідно збільшується частка ворсин з синцитіальними вузликами.

Ключові слова: BAX-залежний апоптоз, трофобласт, ворсинки хоріона, плацента, пологи після 40 тижнів, вагітність.

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INTRODUCTION / ВСТУП

The relevance of studying the molecular mechanisms that regulate apoptosis in placental tissues, especially in the later stages of pregnancy, is crucial for understanding this organ's normal and pathological functioning [1, 2, 3]. Apoptosis, or programmed cell death, is essential for maintaining tissue homeostasis, ensuring normal placental function and adequate metabolism between mother and fetus [4]. One of the main proteins that regulate apoptosis is BAX, a molecule that is actively involved in the initiation of this process through the activation of caspases [5, 6].

Trophoblasts, the cells lining the chorionic villi of the placenta, are crucial for the functioning of this organ, as they ensure close contact with the maternal vascular system, providing for the exchange of gases and nutrients and removal of metabolic products [7, 8]. Maintaining the viability of these cells throughout pregnancy is critical for the normal development of the fetus [9, 10]. However, at specific points in pregnancy (in particular at the final stage – after 40 weeks), changes in apoptosis mechanisms may be associated with the initiation of labor and the adaptation of the placenta to changes in hormonal levels and blood circulation [11].

Growing research in the field of molecular morphology allows us to study in more detail the expression of BAX in placental chorionic villi trophoblasts in late pregnancy [12, 13]. This opens up new possibilities for understanding the role of apoptosis in normal physiological processes, as well as in pathological conditions that may occur at the end of pregnancy, such as placental insufficiency, preterm labor, or other complications [14, 15].

The study aimed to determine by immunohistochemical method the features of BAX-dependent apoptosis in the trophoblast of the placental chorionic villi at delivery after 40 weeks.

MATERIALS AND METHODS

The placental material (pieces from the intermediate zone from the fetal plate to the basal plate) was fixed for 22–24 hours in a neutral buffered (Lilly) 10% aqueous formalin solution. Then, the fixed placental material was dehydrated in an ascending alcohol series (from 50 degrees to "absolute" alcohol) and embedded in paraffin at 58 °C.

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visualize reaction results with diaminobenzidine dye (it gives a clear brown color to the locations of the studied antigens).

Along with the descriptive method of histopathological examination, we also performed computer morphometry on previously obtained digital copies of optical microscopic tissue images (Delta Optical Evolution 100 microscope – planachromatic objectives in accordance with the required optical magnification – and Olympus SP550UZ digital camera with an adapter).

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The obtained digital data were processed using statistical methods. In particular, with the help of a legal copy of the computer program for statistical calculations PAST v 4.17, a preliminary test for the normality of the distribution was performed using the Shapiro–Wilk test. According to this criterion, the hypothesis of normality of distribution was not rejected (at p=0.05) for all the studied statistical samples; thus, parametric statistical analysis methods were used: calculation of the arithmetic mean and its error, unpaired two-sided Student's test. In addition to the Student's test, the non-parametric Mann–Whitney test was also used, but statistical significance was reported only for the Student's test.

RESULTS AND DISCUSSION

As can be seen from Figure 1, in childbirth after 40 weeks of gestation, there are significant amounts of the so-called "syncytial nodules," which look like dark purple clusters (these are trophoblast nuclei in a state of apoptosis) with an attachment to choroidal villi.

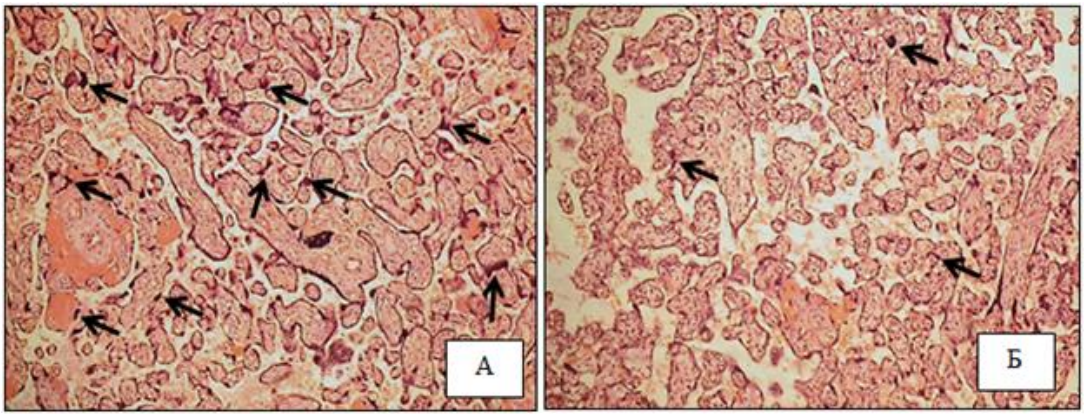

Figure 1 – Syncytial nodules of the chorionic villi of the placenta (examples are shown by arrows)

A) Delivery after 40 weeks of gestation B) Physiologic pregnancy and delivery. Hematoxylin and eosin staining. Obj: 4x, O.10x (optical magnification 40x)

To quantify the "syncytial nodules," the morphometric indicator "The proportion (in ‰ – ppm) of placental chorionic villi with syncytial nodules" was used. The average results of calculations of this indicator are shown in Table 1.

Table 1 shows that the proportion of chorionic villi of the placenta with "syncytial nodules" in deliveries after 40 weeks of gestation is not only greater compared to physiological pregnancy and delivery, but it is more than 10 times higher. It should be noted that "syncytial nodules" in both study groups were recorded in all types of villi studied: stem, intermediate, and terminal. The size of the nodules varied in both study groups; they also differed in the number of nuclei: from 12 to 44 per nodule, but no differences were found between the study groups in terms of the size of the nodules and the number of nuclei in them ($p > 0.05$).

Table 1 – The proportion (in ‰) of chorionic villi of the placenta with syncytial nodules in labor after 40 weeks compared to physiological pregnancy and labor (M±m)

Indicator	Childbirth after 40 weeks of pregnancy (n=30)	Physiological pregnancy and childbirth (n=30)
Proportion of chorionic villi of the placenta with syncytial nodules (‰)	21.8±0.36*	1.9±0.07

*Notes: * Difference in mean trends between the study groups p<0.05 (Student's t-test)*

Since, based on the above data, it was expected that at delivery after 40 weeks, trophoblasts should have manifestations of trophoblast death, appropriate research methods were used, among which preference was given to those immunohistochemical methods that allow detecting changes in the regulation of the so-called BAX-dependent apoptosis, in particular, the immunohistochemical method of detecting the pro-apoptotic protein BAX and its main antagonist, the antiapoptotic protein Bcl-2.

The results of the quantitative assessment of immunohistochemical staining for the pro-apoptotic protein BAX in the trophoblast of the placental chorionic villi at delivery after 40 weeks vs. physiological pregnancy and delivery are shown in Table 2.

Table 2 – The optical density of immunohistochemical staining for the pro-apoptotic protein BAX in the trophoblast of the placental chorionic villi in labor after 40 weeks vs. physiological pregnancy and labor (M±m)

Indicator	Childbirth after 40 weeks of pregnancy (n=30)	Physiological pregnancy and childbirth (n=30)
The optical density of immunohistochemical staining for the pro-apoptotic protein BAX in the trophoblast of the placental chorionic villi (unit opt. density)	0.34±0.013*	0.18±0.007

*Notes: * Difference in mean trends between the study groups p<0.05 (Student's t-test)*

From the data presented in Table 2, it follows that in labor after 40 weeks, there is a significantly higher (almost two-fold) concentration of pro-apoptotic protein BAX in the cytoplasm of the freestanding trophoblast vs. physiological pregnancy and labor, as evidenced by the average values of the index “Optical density of immunohistochemical staining for pro-apoptotic protein BAX in the trophoblast of the placental chorionic villi” (in relative units of optical density).

As shown in Figure 2, the pro-apoptotic protein BAX was found not only in the trophoblast of the placental chorionic villi but also in the stromal cells of the placental chorionic villi. However, there was no significant difference in the indicator “Optical density

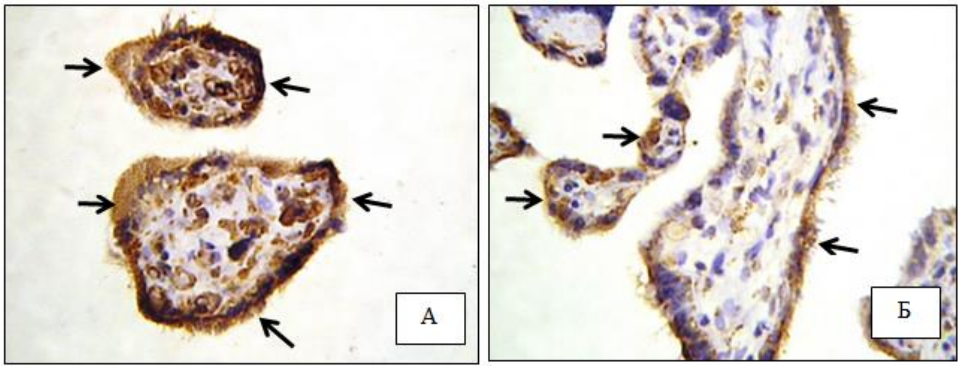

Figure 2 – Pro-apoptotic protein BAX in the trophoblast of the placental chorionic villi (arrows indicate positive reaction sites)

A) Delivery after 40 weeks of pregnancy B) Physiological pregnancy and delivery. Immunohistochemical staining with monoclonal antibodies to BAX-protein (visualization by polymeric detection system with diaminobenzidine) and additional staining of cell nuclei with Girolli hematoxylin. Obj. 40x, O.10x (optical magnification 400x)

of immunohistochemical staining for pro-apoptotic protein BAX in stromal cells of placental chorionic villi" ($p > 0.05$).

It is also essential that the main antagonist of BAX protein, the anti-apoptotic protein Bcl-2, was immunohistochemically detected exclusively in the trophoblast of choroidal villi, and stromal cells did not show positive immunohistochemical staining for Bcl-2 protein at all.

The results of quantitative measurements of immunohistochemical staining for Bcl-2 protein are shown in Table 3.

Table 3 – The optical density of immunohistochemical staining for anti-apoptotic protein Bcl-2 in the trophoblast of placental chorionic villi in labor after 40 weeks compared to physiological pregnancy and labor (M±m)

Indicator	**Childbirth after 40 weeks of pregnancy (n=30)**	**Physiological pregnancy and childbirth (n=30)**
The optical density of immunohistochemical staining for anti-apoptotic protein Bcl-2 in the trophoblast of placental chorionic villi (opt. density unit)	0.15±0.006*	0.24±0.008

*Notes: * Difference in mean trends between the study groups $p<0.05$ (Student's t-test)*

Thus, according to the indicator "Optical density of immunohistochemical staining for the anti-apoptotic protein Bcl-2 in the trophoblast of the placental chorionic villi" (in relative units of optical density) in labor after 40 weeks, the concentration of the anti-apoptotic protein Bcl-2 in the trophoblast of the placental chorionic villi is significantly lower compared to physiological pregnancy and labor – by 1.6 times.

Figure 3 illustrates this pattern.

Thus, from the point of view of molecular regulation of apoptosis in the trophoblast of the placental chorionic villi at delivery after 40 weeks compared to physiological pregnancy and delivery, conditions are created for enhanced trophoblast death by BAX-dependent apoptosis, since there is an increase in the concentration of the pro-apoptotic protein BAX, while the concentration of its main antagonist, Bcl-2, decreases markedly.

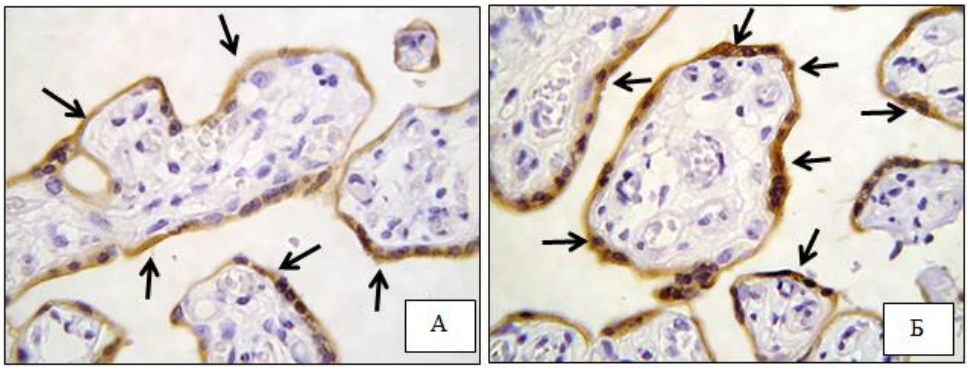

Figure 3 – Anti-apoptotic protein Bcl-2 in the trophoblast of the placental chorionic villi (arrows indicate positive reaction sites)

A) Delivery after 40 weeks of gestation B) Physiologic pregnancy and delivery. Immunohistochemical staining with monoclonal antibodies to Bcl-2 protein (visualization by polymeric detection system with diaminobenzidine) and additional staining of cell nuclei with Girome hematoxylin. Obj. 40x, O.10x (optical magnification 400x)

CONCLUSIONS

At delivery after 40 weeks, the molecular processes of BAX-dependent apoptosis are activated in the placental trophoblast, and the proportion of villi with syncytial nodules increases accordingly.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

It is related to the elucidation of other aspects of trophoblast death in the chorionic villi of the placenta at delivery after 40 weeks, primarily in relation to calcium deposits and placental fibrinoid deposits.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

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None.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The author declares no conflict of interest.

ARTIFICIAL INTELLIGENCE DISCLOSURE / ВИКОРИСТАННЯ ШТУЧНОГО ІНТЕЛЕКТУ

The authors confirm that no artificial intelligence-based technologies were utilized in the writing or editing of the manuscript.

REFERENCES/СПИСОК ЛІТЕРАТУРИ

1. Aplin JD, Jones CJP. Cell dynamics in human villous trophoblast. *Hum Reprod Update*. 2021;27(5):904-922. https://doi.org/10.1093/humupd/dmab015
2. Blecher Y, Michaan N, Baransi S, Baruch Y, Yogev Y. Against medical advice for labor induction due to post-term pregnancies - the impact on pregnancy outcome. *J Matern Fetal Neonatal Med*. 2022;35(20):3979-3983. https://doi.org/10.1080/14767058.2020.1845645
3. Carroll A, Desforges M, Jones CJP, Heazell AEP. Morphological and functional changes in placentas from prolonged pregnancies. *Placenta*. 2022;125:29-35. https://doi.org/10.1016/j.placenta.2022.01.009
4. Gawrys B, Trang D, Cheng W. Management of Late-Term and Postterm Pregnancy. *Am Fam Physician*. 2024;110(4):378-384.
5. Gokalp-Ozkorkmaz E, Asir F, Basaran SO, Agacayak E, Sahin F, Kaya S, et al. *Proceedings.* 2018;2:1548. https://doi.org/10.3390/proceedings2251548
6. Ilika VV, Harvasiuk OV. [Peculiarities of cell regulation processes of trophoblast in chorioamnionitis on the background of iron deficiency anemia of pregnant women]. *Journal of Marine Medicine*. 2021;3:74-81. http://dx.doi.org/10.5281/zenodo.5593346
7. Kojima J, Ono M, Kuji N, Nishi H. Human Chorionic Villous Differentiation and Placental Development. *Int J Mol Sci*. 2022;23(14):8003. https://doi.org/10.3390/ijms23148003
8. Kozar OM, Kalinovska IV. [Risk factors for prolonged pregnancy beyond 40 weeks]. *Bukovinian Medical Herald.* 2023;27(4):39-46. https://doi.org/10.24061/2413-0737.27.4.108.2023.9
9. Lee YS, Kalimuthu K, Park YS, Luo X, Choudry MHA, Bartlett DL, et al. BAX-dependent mitochondrial pathway mediates the crosstalk between ferroptosis and apoptosis. *Apoptosis*. 2020;25(9-10):625-631. https://doi.org/10.1007/s10495-020-01627-z
10. Li H, Peng H, Hong W, Wei Y, Tian H, Huang X, et al. Human Placental Endothelial Cell and Trophoblast Heterogeneity and Differentiation Revealed by Single-Cell RNA Sequencing. *Cells*. 2022;12(1):87. https://doi.org/10.3390/cells12010087
11. Ranjbar A, Mehrnoush V, Darsareh F, Pariafsay F, Shirzadfardjahromi M, Shekari M. The Incidence and Outcomes of Late-Term Pregnancy. *Cureus*. 2023;15(1):e33550. https://doi.org/10.7759/cureus.33550
12. Tokar P. Histochemical and immunohistochemical features of differentiated trophoblast in chorionic villi of the placenta in preterm labor. *Neonatol. hìr. perinat. med.* 2024;14(1(51):84-90. https://doi.org/10.24061/2413-4260.XIV.1.51.2024.12
13. Tsakiridis I, Mamopoulos A, Athanasiadis A, Dagklis T. Induction of Labor: An Overview of Guidelines. *Obstet Gynecol Surv*. 2020;75(1):61-72. https://doi.org/10.1097/ogx.0000000000000752
14. Xiao Z, Yan L, Liang X, Wang H. Progress in deciphering trophoblast cell differentiation during human placentation. *Curr Opin Cell Biol*. 2020;67:86-91. https://doi.org/10.1016/j.ceb.2020.08.010
15. Yang L, Liang P, Yang H, Coyne CB. Trophoblast organoids with physiological polarity model placental structure and function. *J Cell Sci*. 2024;137(5):jcs261528. https://doi.org/10.1242/jcs.261528

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