American Journal of Medicine and Medical Sciences 2025, 15(11): 4099-4104
DOI: 10.5923/j.ajmms.20251511.77

Immunohistochemical Features of Angiogenesis in Malignant Ovarian Tumors (Review Article)

Akhmedov Amed Suyunovich, Oripov Firdavs Suratovich*

Samarkand State Medical University Samarkand, Uzbekistan

Abstract This review article presents an analysis of the immunohistochemical characteristics of angiogenesis in malignant ovarian tumors. The paper describes the role of angiogenesis in the development and progression of the tumor process, and also discusses the key molecular and cellular mechanisms that underlie it. The review includes an analysis of immunohistochemical markers of angiogenesis, such as VEGF, CD31, CD34, and their relationship with tumor progression and disease prognosis. Immunohistochemical analysis methods, their advantages, prospects for antiangiogenic therapy, and possible innovative approaches to research in this area are also discussed.

Keywords Angiogenesis, Immunohistochemistry, Ovarian tumors, VEGF, CD31, CD34, Antiangiogenic Therapy

Angiogenesis, the process of forming new blood vessels, plays a key role in the development and progression of malignant tumors, including ovarian cancer [12]. Under normal physiological conditions, angiogenesis is tightly regulated; however, in the context of tumor growth, it becomes pathological, promoting unlimited nourishment of tumor cells and metastasis [13]. The study of angiogenic mechanisms and their immunohistochemical characteristics in malignant ovarian tumors is of significant scientific and clinical interest [6].

Malignant ovarian tumors occupy one of the leading positions among oncological diseases of the female reproductive system, being characterized by high mortality and a significant prevalence rate [26]. According to the World Health Organization, approximately 300,000 new cases of ovarian cancer are diagnosed annually, with mortality reaching 185,000 deaths per year. The high lethality is primarily due to late diagnosis and the absence of specific symptoms in the early stages of the disease, which complicates timely treatment [1].

The progression of malignant ovarian tumors is closely associated with active angiogenesis, which provides the tumor with the necessary resources for growth and metastasis. Understanding the molecular mechanisms and immunohistochemical features of angiogenesis may not only contribute to earlier diagnosis but also open new therapeutic opportunities [15]. In particular, anti-angiogenic therapy, aimed at inhibiting the growth of new vessels, represents a promising direction in the treatment of malignant ovarian tumors.

* Corresponding author:
sammi-xirurgiya@yandex.com (Oripov Firdavs Suratovich)
Received: Oct. 18, 2025; Accepted: Nov. 3, 2025; Published: Nov. 24, 2025
Published online at http://journal.sapub.org/ajmms

In light of the above, the study of immunohistochemical markers of angiogenesis in the context of ovarian cancer is a relevant task of modern oncology, with significant potential to improve diagnostics and develop effective treatment methods for this disease [37].

Angiogenesis is a fundamental biological phenomenon that plays a critical role in tissue growth and development, wound healing, and reproductive processes [41]. In the context of tumor growth, angiogenesis acquires special importance, as it provides the tumor with the necessary resources for rapid progression and metastasis.

1. Biological Basis of Angiogenesis

Angiogenesis is a vital physiological process that involves the formation of new blood vessels from pre-existing ones [34]. It plays a crucial role in tumor growth and progression, and the balance between angiogenic and anti-angiogenic factors is key to controlling tumor angiogenesis. Vascular endothelial growth factor (VEGF), Notch signaling, angiopoietins, and other mediators play central roles in the regulation of this process [24,12,6].

This process is finely regulated by a complex network of pro-angiogenic and anti-angiogenic factors, with VEGF being one of the most prominent molecules — first characterized by Napoleone Ferrara. Understanding the molecular pathways involved in tumor angiogenesis is essential for developing new anticancer therapies targeting tumor vasculature.

Growth factors (GFs) play a key role in the development of angiogenesis, an essential process for tissue repair and regeneration. These include major molecules such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) [19]. Studies have shown that multiple

GF delivery systems are more effective in promoting the development of stable and mature blood vessels compared to single or sustained-release systems, although they may present complexity and potential interactions [31].

It has been demonstrated that concentrated growth factors (CGFs) derived from blood contain important pro-angiogenic molecules such as VEGF and TGF-β1, which promote endothelial cell migration and tubule formation, indicating their potential in therapeutic vasculogenesis for tissue regeneration [9].

Growth hormone (GH) also plays a crucial role in ovarian angiogenesis by influencing factors such as VEGF-A, IGF-I, and steroids, which are essential for folliculogenesis and luteal function [14]. Angiopoietins (Ang) interact with Tie2 receptors, controlling the maturation and stabilization of new blood vessels. Conversely, endostatin and thrombospondin are anti-angiogenic factors that inhibit angiogenesis by suppressing endothelial cell proliferation and inducing apoptosis.

Understanding the roles of these factors in angiogenesis is critical for developing therapeutic approaches aimed at correcting angiogenic dysregulation in diseases such as cancer and cardiovascular disorders [25].

Hypoxia, frequently observed in tumor tissues, serves as a powerful trigger for angiogenesis. It induces the expression of hypoxia-inducible factor 1 (HIF-1), which activates the transcription of genes encoding angiogenic factors, including VEGF. This process initiates a cascade of events leading to the formation of new blood vessels [40].

Moreover, the tumor microenvironment, composed of various cell types such as fibroblasts, macrophages, and immune cells, actively participates in the regulation of angiogenesis through the secretion of pro-angiogenic cytokines and growth factors.

2. Angiogenesis in Malignant Ovarian Tumors

Angiogenesis plays a crucial role in ovarian tumor growth by promoting the formation of new blood vessels that supply oxygen and nutrients to the tumor tissue [37,1]. Various angiogenic factors and signaling pathways are involved in the development of tumor vascularization and metastasis in ovarian cancer [23]. Studies have shown that angiogenesis-related genes (ARGs) are differentially expressed in patients with ovarian cancer, influencing prognosis and the degree of immune cell infiltration in the tumor microenvironment [47,6].

Moreover, paracrine pathways involving matrix metalloproteinase-1 (MMP1) and protease-activated receptor-1 (PAR1) have been identified as key stimulators of angiogenesis in ovarian cancer, representing potential therapeutic targets. Inhibition of vasculogenic mimicry (VM) — an alternative mechanism of tumor vascularization — is also considered a promising strategy to counteract angiogenesis and improve patient outcomes.

Comparative analysis of angiogenesis in benign and malignant ovarian tumors reveals striking differences [37]. In benign tumors, angiogenesis is more controlled and balanced, with vessels exhibiting normal structure and functionality [39]. The levels of pro-angiogenic factors are generally lower in benign lesions, as they do not require intensive vascular growth. In contrast, malignant ovarian tumors show intense and unregulated angiogenesis, with abnormal vessel morphology that facilitates tumor progression and metastasis [38]. Hypoxia plays a major role in this process, inducing angiogenesis through the activation of hypoxia-inducible factor 1 (HIF-1).

Thus, angiogenesis in malignant ovarian tumors has a more aggressive and destructive nature compared to benign neoplasms. These differences in angiogenic patterns may serve as a foundation for developing diagnostic biomarkers and targeted therapeutic strategies aimed at suppressing pathological vascular growth in ovarian cancer.

3. Main Immunohistochemical Markers of Angiogenesis

The main immunohistochemical markers of angiogenesis include CD31, CD34, and caveolin-1 [7] [34] [2]. These markers are crucial for visualizing and assessing vascular proliferation and neovascularization in various tissues, including tumors and inflammatory lesions. Immunohistochemical markers such as VEGF and its receptors, along with CD31 and CD34, are essential for evaluating angiogenesis in ovarian tumors, particularly malignant ones.

VEGF and its receptors play a key role in stimulating angiogenesis by promoting endothelial cell growth and survival, which are necessary for the formation of new blood vessels in tumors [29]. Activation of VEGF receptors triggers intracellular signaling pathways that enhance angiogenesis and increase vascular permeability. Studies have shown that the expression of VEGF and its receptors often correlates with tumor aggressiveness and poor prognosis. CD31 and CD34 are widely used markers for identifying endothelial cells and assessing microvessel density (MVD) in tumor tissues [17].

CD31 is particularly reliable for identifying vascular structures in tumor samples, with higher expression levels associated with increased angiogenesis and more aggressive clinical behavior.

CD34, expressed on the surface of endothelial cells, is also associated with enhanced angiogenesis and malignant tumor progression. Caveolin-1 (Cav-1) plays a crucial role in the angiogenesis of malignant tumors [10,5,43,27,22]. It has been shown to positively regulate angiogenesis by coordinating VEGF-induced processes, promoting neovascularization, and enhancing endothelial cell differentiation. Cav-1 expression correlates with the formation of vascular mimicry (VM), contributing to tumor progression and resistance to anti-angiogenic therapy. In Kaposi's sarcoma, suppression of Cav-1 by viral interleukin-6 (vIL-6) leads to enhanced angiogenesis and oncogenesis through activation of AKT signaling. These findings highlight the importance of Cav-1 in modulating angiogenesis in various malignancies, making it a potential therapeutic target for inhibiting tumor growth and metastasis.

Caveolin-1 immunostaining shows intense positivity in small and medium-sized vessels, making it a valuable marker for detecting newly formed blood vessels [35]. Overall, these markers play an important role in understanding the mechanisms of angiogenesis and may assist in developing diagnostic and therapeutic strategies for various vascular and neoplastic diseases [20].

4. The Relationship of Markers with Tumor Progression and Disease Prognosis

Immunohistochemical markers of angiogenesis, such as VEGF, CD31, and CD34, have significant prognostic value in ovarian tumors. High expression levels of these markers are often associated with adverse clinical outcomes, including increased tumor aggressiveness, a higher likelihood of metastasis, and reduced survival rates.

VEGF expression in ovarian tumor tissues is particularly important, as elevated levels are linked to higher malignancy, invasiveness, and decreased patient survival. This makes VEGF and its receptors valuable targets for anti-angiogenic therapy.

Moreover, the markers CD31 and CD34 can be used to assess microvessel density (MVD), providing insight into the extent of angiogenesis within tumor tissue. A high MVD level indicates active angiogenesis and is correlated with more aggressive tumor behavior and poor prognosis.

Ultimately, these immunohistochemical markers of angiogenesis play a crucial role in understanding the biological behavior of malignant ovarian neoplasms, aiding in diagnosis, prognosis, and the development of new therapeutic strategies aimed at suppressing pathological angiogenesis and improving patient outcomes.

5. Methods of Immunohistochemical Analysis

Immunohistochemical analysis is indeed a valuable method for studying protein expression in tissues, particularly for investigating angiogenesis markers in ovarian tumors. Studies have demonstrated the importance of immunohistochemistry in differentiating between benign and malignant epithelial ovarian tumors based on angiogenic characteristics [30]. Moreover, the expression of specific markers such as ER, PR, and HER2/neu in epithelial ovarian tumors has been shown to correlate with various clinical and pathological parameters, highlighting the significance of immunohistochemical evaluation in understanding the prognosis of ovarian cancer [28].

In addition, the expression of certain markers such as p53, p16, and Ki-67 has been recognized as useful for the differential diagnosis of serous ovarian/tubo-ovarian tumors, further emphasizing the role of immunohistochemistry in assessing tumor characteristics and prognosis [8].

6. Advantages and Limitations of Different Methods

Different methods of immunohistochemical (IHC) analysis have their own advantages and limitations. Enzyme-based immunohistochemistry (IHC-ER) is characterized by its simplicity, quantitative capability, long shelf life, and low cost. However, it requires careful optimization of experimental conditions, has limited sensitivity and resolution, and may produce background staining. On the other hand, fluorescence-based immunohistochemistry (IHC-IF) provides high sensitivity, multiplexing capability, high resolution, and quantitative assessment. Nevertheless, it is prone to photobleaching, requires more complex optimization, and is more expensive [16].

In studies of angiogenesis mechanisms in malignant ovarian tumors, it has been found that angiogenesis is regulated by cellular and molecular mechanisms. Hypoxia and hypoxia-inducible factor 1 (HIF-1), along with the tumor microenvironment, play key roles in the activation of angiogenesis. Hypoxia, caused by oxygen deprivation, stimulates the activation of HIF-1. HIF-1 is a transcription factor that normally undergoes degradation but becomes stabilized under hypoxic conditions. In the nucleus, HIF-1 binds to hypoxia response elements (HREs) and activates the transcription of genes, including VEGF, that promote angiogenesis.

7. The Influence of Genetic and Epigenetic Factors on Angiogenesis

Genetic mutations and epigenetic modifications indeed play a crucial role in the regulation of angiogenesis in ovarian tumors. Epigenetic alterations such as DNA methylation and histone modifications have been identified as key factors influencing drug resistance in ovarian cancer [4,42]. These modifications can affect the expression of tumor suppressor genes such as BARD1, thereby contributing to resistance against VEGF-targeted therapies [21].

Moreover, epigenetic alterations in omental stem cells derived from adipose tissue create a favorable microenvironment for chemoresistance and tumor dissemination in ovarian cancer [3]. Epigenetic dysregulation, including DNA methylation and histone modification, is considered a major contributor to oncogenesis and tumor maintenance, highlighting the importance of epigenetic markers in angiogenesis and the potential use of “epidrugs” in cancer therapy.

Understanding the role of genetic mutations and epigenetic modifications in the regulation of angiogenesis may help in developing novel therapeutic strategies for the treatment of ovarian tumors.

8. Prognostic Significance of Immunohistochemical Markers

Immunohistochemical markers of angiogenesis in malignant ovarian tumors include smooth muscle actin (SMA) [36], CD34, nestin [32], PDGF-B [11], and osteopontin [18]. The expression of smooth muscle actin is typically low in malignant tumors, indicating a higher microvessel density (MVD). CD34 is used for the quantitative assessment of microvessels, which are more densely distributed in malignant ovarian tumors. Nestin, a stem cell marker, is expressed in epithelial ovarian carcinoma (EOC) and correlates with poor prognosis, suggesting its potential as a therapeutic target for tumor angiogenesis. Evaluation of MVD with PDGF-B positivity and nestin expression helps identify highly active angiogenic malignant ovarian tumors. Osteopontin, when combined with CA125 and HE4, enhances the differential diagnosis between malignant and benign ovarian tumors. These markers play a crucial role in assessing angiogenesis and predicting the prognosis of malignant ovarian neoplasms.

9. Anti-angiogenic Therapy: VEGF Inhibitors and Other Agents

Anti-angiogenic therapy holds great promise in the treatment of malignant ovarian tumors by inhibiting the formation of new blood vessels essential for tumor growth. Studies emphasize the central role of the VEGF/VEGFR signaling pathway in tumor vascularization [26,45]. Anti-angiogenic agents such as bevacizumab have demonstrated the ability to reduce tumor volume and improve patient survival when combined with chemotherapy [44].

However, challenges such as drug resistance and a limited number of prognostic biomarkers hinder the full effectiveness of anti-angiogenic drugs in ovarian cancer treatment [47]. Although these therapies improve progression-free survival, the overall survival benefits remain limited, necessitating careful patient selection due to the increased risk of serious side effects such as hypertension and gastrointestinal perforation [46].

Thus, while anti-angiogenic therapy represents a promising strategy, its efficacy in treating malignant ovarian tumors requires further optimization and a personalized approach to maximize therapeutic benefits.

10. Conclusions

A review of the literature and conducted studies on immunohistochemistry and angiogenesis in malignant ovarian tumors allows us to draw the following key conclusions.

Angiogenesis plays a crucial role in the development and progression of malignant ovarian tumors. Dysregulation of angiogenic processes, associated with high expression of angiogenic factors, promotes intensive tumor growth, invasion, and metastasis. Immunohistochemical markers of angiogenesis have high prognostic significance.

The expression of markers such as VEGF, CD31, and CD34 allows for the assessment of angiogenic activity and prediction of disease progression in patients with malignant ovarian tumors. Anti-angiogenic therapy represents a promising approach in the treatment of ovarian tumors. VEGF inhibitors and other agents targeting angiogenesis suppression can improve treatment outcomes and patient prognosis.

11. Future Research Perspectives

Further research in the field of immunohistochemistry and angiogenesis in malignant ovarian tumors should focus on:

Identifying new angiogenic markers for prognosis;

Studying mechanisms of resistance to anti-angiogenic therapy to overcome drug resistance;

Developing innovative approaches for investigating tumor heterogeneity and creating personalized therapeutic strategies.

Promising innovative approaches include multiplex immunohistochemical analysis to improve diagnostic precision, molecular imaging methods to visualize angiogenic processes and identify new therapeutic targets, and single-cell sequencing to study tumor cell population heterogeneity and uncover novel mechanisms of angiogenesis regulation.

Such studies have the potential to significantly enhance diagnosis, prognosis, and treatment of malignant ovarian tumors, ultimately improving patient outcomes.

REFERENCES

[1] Agarwal A. et al. Identification of a metalloprotease-chemokine signaling system in the ovarian cancer microenvironment: implications for antiangiogenic therapy // Cancer research. – 2010. – T. 70. – №. 14. – C. 5880-5890.

[2] Al-Keilani M. S. et al. Immunohistochemical expression of GRP78 in relation to angiogenesis markers VEGF-a and CD31 and other histopathological parameters in NSCLC. – 2019.

[3] Aspriţoiu V. M. et al. Epigenetic regulation of angiogenesis in development and tumors progression: potential implications for cancer treatment // Frontiers in Cell and Developmental Biology. – 2021. – T. 9. – C. 689962.

[4] Bayraktar E. et al. Epigenetic regulation of BARD1 confers resistance to anti-VEGF therapy in ovarian cancer // Cancer Research. – 2023. – T. 83. – №. 7_Supplement. – C. 6001-6001.

[5] Bernatchez P. Endothelial caveolin and its scaffolding domain in cancer // Cancer and Metastasis Reviews. – 2020. – T. 39. – C. 471-483.

[6] Bhardwaj V. et al. Neo-vascularization-based therapeutic perspectives in advanced ovarian cancer // Biochimica et Biophysica Acta (BBA)-Reviews on Cancer. – 2023. – С. 188888.

[7] Biagioni A., Andreucci E. Immunohistochemistry for VM Markers // Vasculogenic Mimicry: Methods and Protocols. – New York, NY : Springer US, 2022. – С. 141-152.

[8] Binch A., Snuggs J., Le Maitre C. L. Immunohistochemical analysis of protein expression in formalin fixed paraffin embedded human intervertebral disc tissues // JOR spine. – 2020. – Т. 3. – №. 3. – С. e1098.

[9] Calabriso N. et al. Angiogenic properties of concentrated growth factors (CGFs): the role of soluble factors and cellular components // Pharmaceutics. – 2021. – Т. 13. – №. 5. – С. 635.

[10] Chen W. et al. Caveolin-1 promotes tumor cell proliferation and vasculogenic mimicry formation in human glioma // Brazilian Journal of Medical and Biological Research. – 2021. – Т. 54. – С. e10653.

[11] Czekierdowska S. et al. Proliferation and maturation of intratumoral blood vessels in women with malignant ovarian tumors assessed with cancer stem cells marker nestin and platelet derived growth factor PDGF-B // Ginekologia Polska. – 2017. – Т. 88. – №. 3. – С. 120-128.

[12] da Silva Francisconi n., poletto a. g., rivero e. r. c. evaluation of the role of angiogenesis in the development and progression of oral cancer // Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. – 2023. – Т. 136. – №. 1. – С. e60-e61.

[13] Delgado-Bellido D. et al. VE-Cadherin in cancer-associated angiogenesis: A deceptive strategy of blood vessel formation // International Journal of Molecular Sciences. – 2023. – Т. 24. – №. 11. – С. 9343.

[14] Devesa J., Caicedo D. The role of growth hormone on ovarian functioning and ovarian angiogenesis // Frontiers in endocrinology. – 2019. – Т. 10. – С. 466125.

[15] Flores-Pérez A. et al. Angiogenesis analysis by in vitro coculture assays in transwell chambers in ovarian cancer // MicroRNA and Cancer: Methods and Protocols. – 2018. – С. 179-186.

[16] Gentles L. et al. Integration of computer-aided automated analysis algorithms in the development and validation of immunohistochemistry biomarkers in ovarian cancer // Journal of Clinical Pathology. – 2021. – Т. 74. – №. 7. – С. 469-474.

[17] Gupta A. et al. Comparing subharmonic imaging and immunohistochemical markers of angiogenesis // 2014 IEEE International Ultrasonics Symposium. – IEEE, 2014. – С. 1156-1159.

[18] Horala A. et al. Diagnostic value of serum angiogenesis markers in ovarian cancer using multiplex immunoassay // International Journal of Molecular Sciences. – 2017. – Т. 18. – №. 1. – С. 123.

[19] Hosseini S. A., Shafieian R., Alipour F. Role of growth factors and cytokines in therapeutic angiogenesis // Biomaterials for Vasculogenesis and Angiogenesis. – Woodhead Publishing, 2022. – С. 85-111.

[20] Kargahi N. et al. Immunohistochemically detection of angiogenesis in oral pre-cancerous lesions compared with oral invasive carcinomas // Asian Pacific journal of cancer prevention: APJCP. – 2018. – Т. 19. – №. 7. – С. 1805.

[21] Kelly R. et al. Can epigenetic treatments efficiently revoke the ability of 3D ovarian cancer cells to proliferate, migrate, and invade?. – 2023.

[22] Li W. et al. Viral interleukin-6 encoded by an oncogenic virus promotes angiogenesis and cellular transformation by enhancing STAT3-mediated epigenetic silencing of caveolin 1 // Oncogene. – 2020. – Т. 39. – №. 23. – С. 4603-4618.

[23] Lim D. et al. Angiogenesis and vasculogenic mimicry as therapeutic targets in ovarian cancer // BMB reports. – 2020. – Т. 53. – №. 6. – С. 291.

[24] Lo C. W. et al. IL-6 trans-signaling in formation and progression of malignant ascites in ovarian cancer // Cancer research. – 2011. – Т. 71. – №. 2. – С. 424-434.

[25] Matkar P. N. et al. Friends turned foes: angiogenic growth factors beyond angiogenesis // Biomolecules. – 2017. – Т. 7. – №. 4. – С. 74.

[26] Mei C. et al. Anti-angiogenic therapy in ovarian cancer: Current understandings and prospects of precision medicine // Frontiers in Pharmacology. – 2023. – Т. 14. – С. 1147717.

[27] Mohamed F. E. Z. A., Khalil E. Z. I., Toni N. D. M. Caveolin-1 expression together with VEGF can be a predictor for lung metastasis and poor prognosis in osteosarcoma // Pathology & Oncology Research. – 2020. – Т. 26. – С. 1787-1795.

[28] Mohieldin Z. Y. et al. Immunohistochemical expression of estrogen receptors, progesterone receptors, and human epidermal growth-factor receptor 2/neu in epithelial ovarian tumors // Journal of Medicine in Scientific Research. – 2022. – Т. 5. – №. 3. – С. 309.

[29] Nefedova N. A. et al. Markers of angiogenesis in tumor growth // Arkhiv patologii. – 2016. – Т. 78. – №. 2. – С. 55-63.

[30] Němejcová K. et al. A comprehensive immunohistochemical analysis of 26 markers in 250 cases of serous ovarian tumors // Diagnostic Pathology. – 2023. – Т. 18. – №. 1. – С. 32.

[31] Omorphos N. P. et al. Understanding angiogenesis and the role of angiogenic growth factors in the vascularisation of engineered tissues // Molecular biology reports. – 2021. – Т. 48. – С. 941-950.

[32] Osman W. M., Shash L. S., Ahmed N. S. Emerging role of nestin as an angiogenesis and cancer stem cell marker in epithelial ovarian cancer: immunohistochemical study // Applied Immunohistochemistry & Molecular Morphology. – 2017. – Т. 25. – №. 8. – С. 571-580.

[33] Pazzini J. M. et al. Histochemical and immunohistochemical evaluation of angiogenesis in rabbits (Oryctolagus cuniculus) submitted to skin grafts associated with platelet-rich plasma // Pesquisa Veterinária Brasileira. – 2017. – Т. 37. – С. 1519-1525.

[34] Sanikommu A. et al. Study on molecular basis of cancer induced angiogenesis // Journal of Pharmaceutical Research International. – 2022. – Т. 34. – №. 26A. – С. 85-94.

[35] Seyedmajidi M. et al. Immunohistochemical evaluation of angiogenesis related markers in pyogenic granuloma of gingiva // Asian Pacific Journal of Cancer Prevention. – 2015. – T. 16. – №. 17. – C. 7513-7516.

[36] Srujana S., Quadri S. S. S., Srimani N. Analysis of Tumor Vascularization with Smooth Muscle Actin by Immunohistochemistry—it's Prognostic Significance in Differentiating Benign and Malignant Ovarian Surface Epithelial Tumors. – 2019.

[37] Tang H. et al. Molecular subtypes, clinical significance, and tumor immune landscape of angiogenesis-related genes in ovarian cancer // Frontiers in Oncology. – 2022. – T. 12. – C. 995929.

[38] Treps L., Gavard J. Tumor angiogenesis: when the Tree of Life turns bad // Medecine Sciences: M/S. – 2015. – T. 31. – №. 11. – C. 989-995.

[39] Turner H. E. et al. Angiogenesis in endocrine tumors // Endocrine reviews. – 2003. – T. 24. – №. 5. – C. 600-632.

[40] Viloria-Petit A. et al. Role of Transforming Growth Factor Beta Family in Angiogenesis // Biochemical Basis and Therapeutic Implications of Angiogenesis. – 2017. – C. 75-103.

[41] Wang S. et al. PPA1, an energy metabolism initiator, plays an important role in the progression of malignant tumors // Frontiers in Oncology. – 2022. – T. 12. – C. 1012090.

[42] Wang Y. et al. The emerging roles and therapeutic implications of epigenetic modifications in ovarian cancer // Frontiers in Endocrinology. – 2022. – T. 13. – C. 863541.

[43] Zhang Z. B. et al. Caveolin-1 knockdown decreases SMMC7721 human hepatocellular carcinoma cell invasiveness by inhibiting vascular endothelial growth factor-induced angiogenesis // Canadian Journal of Gastroenterology and Hepatology. – 2020. – T. 2020.

[44] Bazin I., Garin A. Targeted antiangiogenic drugs in the therapy of solid tumors. // Vrach (The Doctor). – 2008. – No. 11. – P. 52–55.

[45] Kedrova A. G. Changing strategies in the treatment of patients with recurrent ovarian cancer: Based on the materials of the 5th International Conference on Gynecologic Oncology held by MD Anderson Cancer Center (Madrid, Spain, February 24–26, 2016). // Tumors of the Female Reproductive System. – 2016. – No. 1. – P. 68–72.

[46] Sahin U., Türeci Ö. Therapy for cancer treatment comprising antibodies against Claudin 18.2. – 2019.

[47] Tsandekova M. R., Porkhanova N. V., Kutilin D. S. Molecular characterization of serous ovarian adenocarcinoma: significance for diagnosis and treatment. // Modern Problems of Science and Education. – 2020. – No. 1. – P. 55–55.