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HSP70 VƏ HSP90 ZÜLALLARININ ENDOMETRİUM KARSİNOMALARININ İNKİŞAFINDA ROLU

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Xülasə. *HSP70 və HSP90 tipli istilik şoku zülallarının endometrium karsinomalarının (endometriumun endometrioid karsinoması, endometriumun seroz karsinoması, endometriumun şəffafhüceyrəli karsinoması) inkişafında rolunu və onların estrogen və progesteron reseptorları ilə əlaqəsini, həmçinin proliferasiya və apoptoz aktivliyində rolunu öyrənmək məqsədilə tədqiqat aparılmışdır. HSP70, HSP90, estrogenlər (ES), progesteron (PR), Ki-67 və p53 zülallarının immunhistokimyəvi analizi məqsədilə endometrium karsinoması şişinin 40 nümunəsi (endometrioid karsinoma – 20, seroz və şəffafhüceyrəli karsinoma – hər birindən – 10) tədqiq edilmişdir.Müqayisə üçün 10 nəfər uşaqlıq leyomioması olan qadının normal toxumasından istifadə edilmişdir.*

HSP70 və HSP90 zülallarının ekspressiyasına həm normal, həm də şiş toxumalarının hər birində rast gəlinmişdir. Neoplastik transformasiya, şişin diferensiasiyası və xərçəng hüceyrələrinin anaplaziyasının sürətlənməsi HSP70 və HSP90 zülalları ekspressiyasının intensivliyinin artımı ilə müşayiət edilmiş, bu zaman reseptor-müsbət hüceyrələrin sayı artmış, nüvə patterninin sitoplazmatik əlamətlərə nisbətən üstünlüyü müşahidə edilmişdir ($p<0,05$). HSP70 və HSP90 zülallarının eyni vaxtda və eyni istiqamətdə aktivləşməsi şiş hüceyrələrində ES və PR ekspressiyasından asılı olmamışdır.

Beləliklə, alınmış nəticələr HSP70 vəHSP90 zülallarının endometrium karsinomasının inkişafında rolunu sübut edir. Onların şiş hüceyrələrindəki ekspressiyasının artması proliferativ aktivliyin güclənməsi, p53-ün ekspressiyası və hüceyrə anaplaziyası ilə korrelyasiya edir. HSP70 və SP90-ın ekspressiyasının variabelliyi onlardan diaqnostik məqsədlə istifadə edilə biləcəyini və müalicə sxeminin fərdiləşdirilməsində əhəmiyyətini sübut edir.

Açar sözlər: *istilik şoku zülalları, endometrium xərçəngi, uşaqlıq xərçəngi*
Ключевые слова: *белки теплового шока, рак эндометрия, рак матки*
Key words: *heat-shock proteins, endometrial carcinoma, uterus cancer*

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THE ROLE OF HSP70 AND HSP90 IN THE ENDOMETRIAL CARCINOMAS PROGRESSION

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Summary. *This study was aimed to determine the role of heat-shock protein Hsp70 and Hsp90 in the progression of endometrial carcinomas (endometrioid, serous, and, clear-cell endometrial carcinoma) and their link with estrogen and progesterone receptors, proliferation and apoptosis activities.*

We used 40 samples of endometrial carcinoma (20 cases of endometrioid carcinomas, 10 – serous carcinomas, and clear-cell carcinomas) for the immunohistochemical study of HSP70, HSP90, ER, PR, Ki-67, and P53. Normal endometrial tissues (n = 10) were taken from women suffering from uterine leiomyoma.

Hsp70 and Hsp90 expressions were present in all cases of both normal and tumoral endometrial tissues. Neoplastic transformation, tumor differentiation, and increased anaplasia of cancer cells were accompanied by the growth of the Hsp70 and Hsp90 expression intensity, the number of receptor-positive cells, and the predominance of the nuclear pattern over the cytoplasmic one ($p<0.05$). Their increased expression in tumoral cells correlates with proliferative activity intensification and p53 expression ($p<0.05$). The Hsp70 and Hsp90 simultaneous and unidirectional activation in tumor tissue does not depend on the ER and PR expression.

Thus, the results demonstrate the Hsp70 and Hsp90 involvement in the endometrial carcinoma progression. Their increased expression in tumoral cells correlates with proliferative activity intensification, p53 expression, and cell anaplasia. The variability of Hsp70 and Hsp90 expression in endometrial carcinomas accents the importance of adding them to diagnostic panels with subsequent treatment personification.

Prognosis of endometrial carcinoma depends on numerous factors, including tumor cells' molecular genetic profile [1]. Nowadays, the therapeutic and prognostic significance of estrogen receptors (ER), progesterone receptors (PR), Ki-67, and p53 expression in the course of malignant tumors of female reproductive organs has been proven [1,2].

Heat-shock proteins (Hsp) or chaperones are potential indicators of initiation and progression of carcinoma. In the human body, they play an essential role in folding and transporting intracellular proteins and counteracting stress factors' negative effects (refolding proteins) [3,4]. In neoplastic cells, they have been involved in inducing the proliferation and inhibition of apoptosis (synthesis of mutant p53), blocking the immune response, and angiogenesis [5-8]. Moreover, they can interact closely with each other and promoting the invasion of tumor cells [9].

In the normal endometrium, chaperones are expressed throughout the menstrual cycle [5,10]. There is both suppression of Hsp90 expression and an increase of Hsp70 expression in the secretion phase. They are involved in maintaining the stability of epithelial cells, embryonic development, ovogenesis, and others [11]. Hsp70 and Hsp90 co-function with ER, participating in their transcription and activity [12]. Significant variations of Hsp70 and Hsp90 expression were found in carcinomas of the female reproductive organs and breast [6]. Pronounced Hsp90 expression is accompanied by overexpression of ER [13]. On the other hand, some studies demonstrate the absence of any relationship between them in carcinoma tissue [10]. Hsp90 expression, observed in 30% of cases, was an indicator of a better prognosis in endometrial carcinomas [6,14]. Moreover, the opposite results were found in the mammary gland [15]. Hsp70 expression (observed in 50% of endometrial carcinoma cases) is associated with a worse prognosis [6,14].

Material and research methods.

Patients and samples

Endometrial tissue samples were obtained from patients who underwent hysterectomy or curettage throughout 2018-2020 at the Gynecology Department of the Sumy Regional Oncology Center (Sumy, Ukraine). We used 40 samples of endometrial carcinoma (20 cases of endometrioid carcinomas (EC), 10 – serous carcinomas (SC), and clear-cell carcinomas (CCC)). All of them were classified and graded according to the World Health Organization recommendations [1]. Normal endometrial tissues (n = 10) were taken from women suffering from uterine leiomyoma. Written informed consents for tissue investigation were obtained from patients. The Institute Bioethics Commission approved the experimental protocol (№ 4/6 of 16/06/2018).

Immunohistochemistry

After histological examination of hematoxylin-eosin stained samples, paraffin blocks were used for the immunohistochemical assay. Serial sections of 5 μm were performed and mounted on 3-aminopropyltriethoxysilane-coated slides. After exposition in the thermostat (57^0C) overnight, deparaffinization, rehydratation, and heat-mediated antigen retrieval were performed utilizing a water bath with "Dewax and HIER Buffer L" ("Thermo scientific") for 30 minutes at 97^0C. Endogenous peroxidase activity was blocked by "UltraVision Hydrogen Peroxidase Block" ("Thermo scientific") for 10 minutes, followed by washing with PBS (pH 7.3). Background staining potentially caused by unspecific binding of antibody proteins was prevented by "UltraVision Protein Block" for 5 minutes. Incubation with the

following panel of antibodies for 30 minutes was used: mouse anti-HSP70 mAb (W27, "Thermo scientific"), rabbit anti-HSP90 pAb ("Thermo scientific"), rabbit anti-ER mAb (SP1, "Thermo scientific"), rabbit anti-PR mAb (YR85, "Thermo scientific"), rabbit anti-Ki-67 mAb (SP6, "Thermo scientific"), and mouse anti-P53 mAb (SP5, "Thermo scientific"). After washing and subsequent amplification of signals by "Primary Antibody Amplifier Quanto" ("Thermo scientific"), the "HRP Polymer Quanto" ("Thermo scientific") were applied and incubated for 10 minutes each at room temperature. Positive stained patterns were visualized by "DAB Quanto" ("Thermo scientific"), controlling the developing color intensity via light microscopy. Subsequently, the DAB reaction was stopped with distilled H_2O as soon as the desired color intensity was obtained. DAB-negative structures were identified by additional counterstaining with Mayer's hematoxylin. Stained sections were mounted.

Evaluation of staining

Three pathologists independently analyzed histological and immunohistochemical staining evaluations. Slides with conflicting evaluations were re-evaluated, and a consensus was reached. The reaction was considered positive if the cells had cytoplasmic and/or nuclear signals for Hsp70 and Hsp90, exclusively nuclear – for ER, PR, Ki-67, and p53. The percentage of receptor-positive cells was scored as the number of receptor-positive cells among the total number of tumor cells. The intensity of stained cells was considered separately. Each indicator was assigned the appropriate number of points – 0-5 for the proportion of colored cells and0-3 – for the intensity of colored cells. Data processing was carried out using the GraphPad Prism® statistics software package, version 6.0. The estimation of the potential differences between the comparable indicators was carried out using Student's t-test. Detection and evaluation of the indicators' links were carried out by the nonparametric Spearman correlation coefficient (r). A p-value of 0.05 (95% confidence) was considered statistically significant.

Research results.

Expression of ER, PR, Ki-67, p53, Hsp70, and Hsp90 in normal endometrium

To establish the peculiarities of the receptors' expression in neoplastic transformation, we first investigated the normal endometrium. Regardless of the menstrual cycle phase, the endometrium's luminal and glandular epithelial cells expressed ER and PR. The endometrium of the proliferation phase had a pronounced expression of ER (94.1 ± 6.5%) and PR (82.5±8.4%) (*Figure 1 – top panel*). Their expression reached its peak in the late phase of proliferation. The secretion phase's endometrium was characterized by a gradual decrease in ER and PR expression with their maximum reduction in the middle phase of secretion (*Figure 2 – top panel*).

More pronounced proliferative activity of the glandular epithelium was observed in the menstrual cycle's proliferation phase (Ki-67 expression was detected in about 20.5% of cells). In the secretion phase, epithelial cells had significantly lower mitotic activity – Ki-67 exhibition was found in about 4.5% of cells. We did not find any cells in the normal endometrium throughout the menstrual cycle expressing p53 (*Figure 1 and Figure 2 – middle panel*).

Nuclear-cytoplasmic expression of Hsp70 and Hsp90 was detected in both phases of the menstrual cycle (*Figure 1 and Figure 2 – bottom panel*). There was a tendency for the signal intensity for Hsp 90 to decrease and Hsp70 to increase in the middle and late secretion phases. We did not find that chaperone expression depended on the menstrual cycle phases, the level of proliferative activity of cells, or the endometrium's sensitivity to female sex hormones ($p>0.05$). A more intense expression was observed in the cytoplasmic pattern of epithelial cells than in the nucleus.

Expression of ER, PR, Ki-67, p53, Hsp70, and Hsp90 in tumoral endometrium

Variable ER and PR expressions in neoplastic cells were detected in all cases of EC tissues (on average 53.8 ± 10.1%, 42.4 ± 6.3%, respectively). It should be noted that grade 1 EC had a more pronounced ER and PR expression, with a gradual decrease along carcinoma dedifferentiation (grade 1 → grade 2 → grade 3) ($p<0.05$) (*Figure 3 – top panel*).

The level of proliferative activity depended on the degree of EC differentiation (on average 35.6 ± 5.4%) – more pronounced expression was detected in grade 2 and grade 3 tumors than in grade 1 carcinomas ($p < 0,05$). The p53 expression was found in single cells of low-grade EC, increasing their number in high-grade EC (grade 2-3) (*Figure 3 - middle panel*).

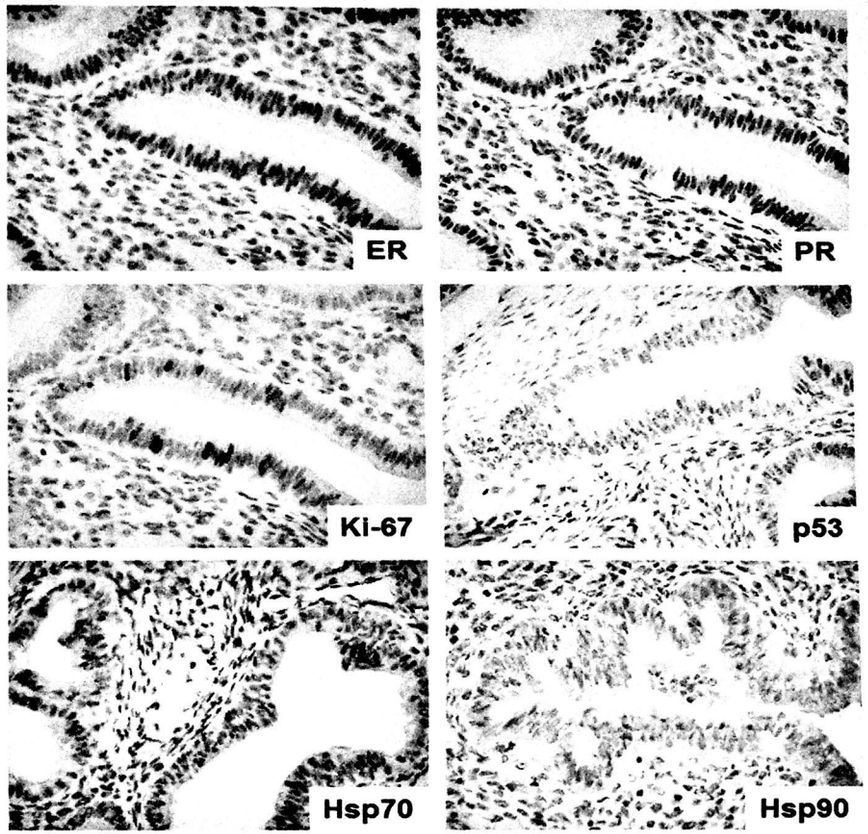

Figure 1. Normal endometrium of proliferation phase: a pronounced expression of ER and PR, moderate expression of Ki-67, no expression of p53, moderate nuclear-cytoplasmic expression of Hsp70 and Hsp90. Expression was evaluated exclusively in the epithelial component of the tissue. Immunohistochemical study of ER, PR, Ki-67, p53, Hsp70, and Hsp90. Magnification x400.

Most EC cases had moderate and pronounced nuclear-cytoplasmic expression of Hsp70 and Hsp90 (*Figure 3 – bottom panel*). Dedifferentiation of carcinoma was accompanied by an increase in receptor expression intensity and the number of receptor-positive cells ($p <0.05$). Moreover, tumor cells' anaplasia progression was reflected in the receptor expression patterns – intensity translocation from the cytoplasm to the nuclei.

However, SC and CCC had more variable receptor expressions. Thus, the SC tissues in the vast majority of cases were ER- and PR-negative (*Figure 4 – top panel*).. Instead, the SC cells' proliferative activity (on average 48.7 ± 9.2%) was significantly higher than their level in normal endometrium and the EC tissues ($p < 0.05$). All SC cases were p53-positive (on average 82.4 ± 6.8% of carcinoma cells) (*Figure 4 – middle panel*In addition, high chaperone activity was detected in all cases of tumors.It was found that SC cells have a more pronounced nuclear expression of Hsp70 and Hsp90 than cytoplasmic (*Figure 4 – bottom panel*).

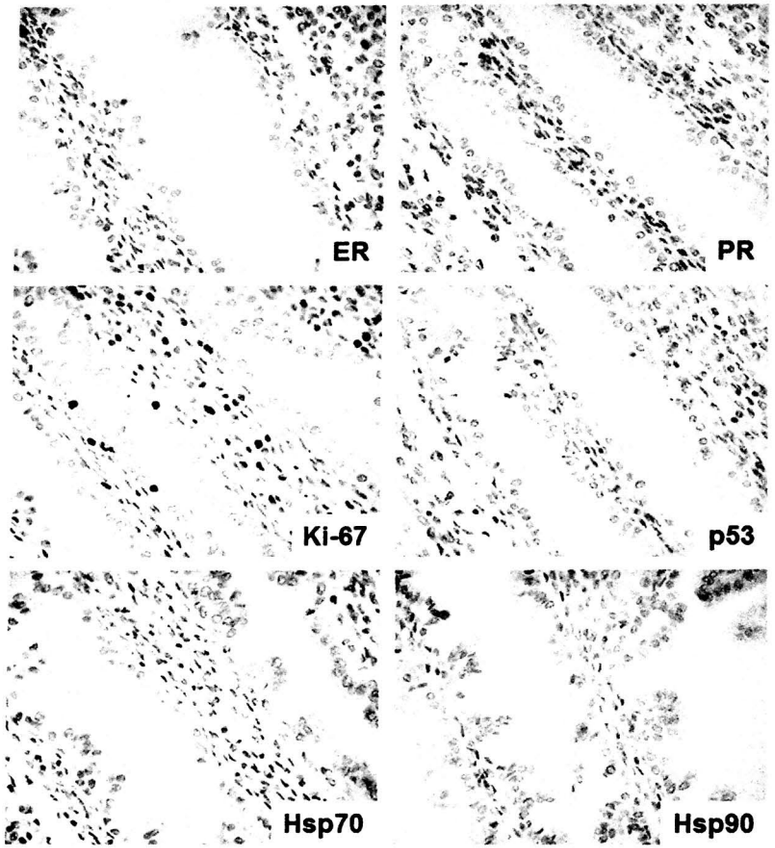

Figure 2. Normal endometrium of secretion phase: an almost complete absence of ER and PR expression, weak expression of Ki-67, no expression of p53, moderate nuclear-cytoplasmic expression of Hsp70 and Hsp90. Expression was evaluated exclusively in the epithelial component of the tissue. Immunohistochemical study of ER, PR, Ki-67, p53, Hsp70, and Hsp90. Magnification x400.

All cases of CCC were ER- and PR-negative (*Figure 5 – top panel*). Instead, they had pronounced cells' proliferative activity (average 52.6 ± 5.8%) and p53 expression (on average 62.6 ± 4.4%) (*Figure 5 – middle panel*). Similar to SC, CCC tumor cells had an intensive expression of both chaperones (Hsp70 and Hsp90) with a significant predominance of the receptor signal in the cell nuclei (*Figure 5 – bottom panel*).

In addition to the aforecited expression of receptors in neoplastic cells, tissue samples' evaluation revealed positively stained cells in the stromal components of both normal and neoplastic endometrial tissues. They were an indicator (positive internal control) of the immunohistochemical study quality, which was especially important in cases with a negative receptor profile of tumor cells.

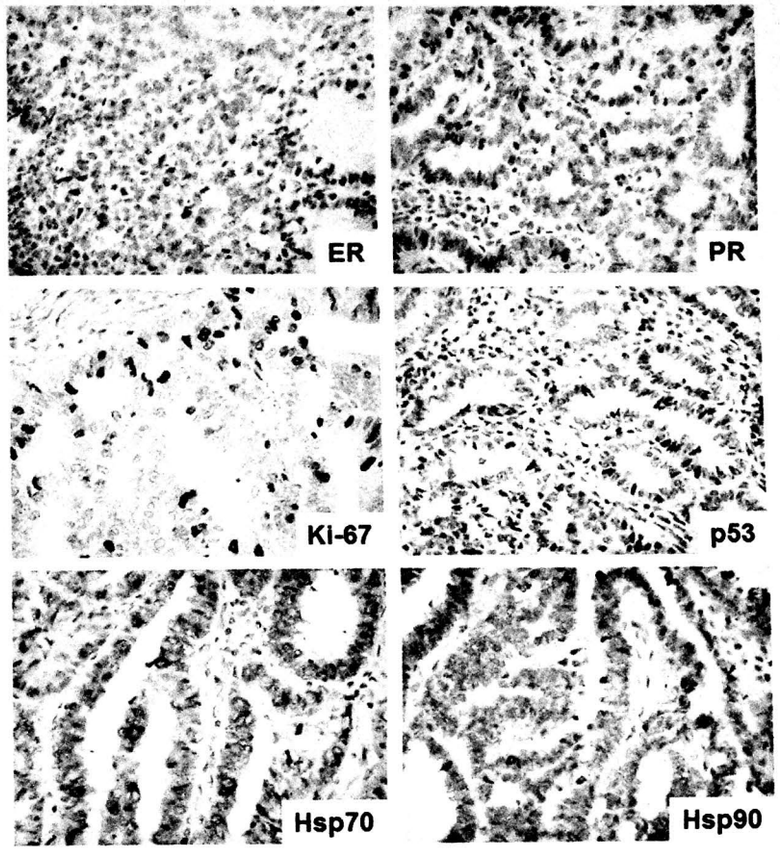

Figure 3. Endometrioid carcinoma: a pronounced ER expression, moderate PR expression, moderate Ki-67 expression, p53 expression in single tumor cells, moderate nuclear-cytoplasmic expression of Hsp70 and Hsp90. Expression was evaluated exclusively in the epithelial component of the tissue. Immunohistochemical study of ER, PR, Ki-67, p53, Hsp70, and Hsp90. Magnification x400.

Comparative analysis of expression in normal and tumor tissues

An immunohistochemical study did not reveal a significant difference in the ER and PR expression in the normal endometrium and neoplastic EC cells ($p > 0.05$). In contrast, SC and CCC tumor cells had significantly lower (mostly negative) steroid hormone receptor expression compared to normal ($p < 0.05$). All types of endometrial carcinoma had more pronounced cell proliferative activity and p53 expression ($p < 0.05$). The highest rates were observed in SC and CCC. The p53 expression was found exclusively in tumor cells and was specific for high-grade EC, SC, and CCC.

Hsp70 and Hsp90 expressions were present in all cases of both normal and tumoral endometrial tissues. Neoplastic transformation, tumor differentiation, and increased anaplasia of cancer cells (especially in SC and CCC) are accompanied by the growth of the Hsp70 and Hsp90 expression intensity, the number of receptor-positive cells, and the predominance of the nuclear pattern over the cytoplasmic one ($p < 0.05$). There is no relationship between the normal and tumoral cells'

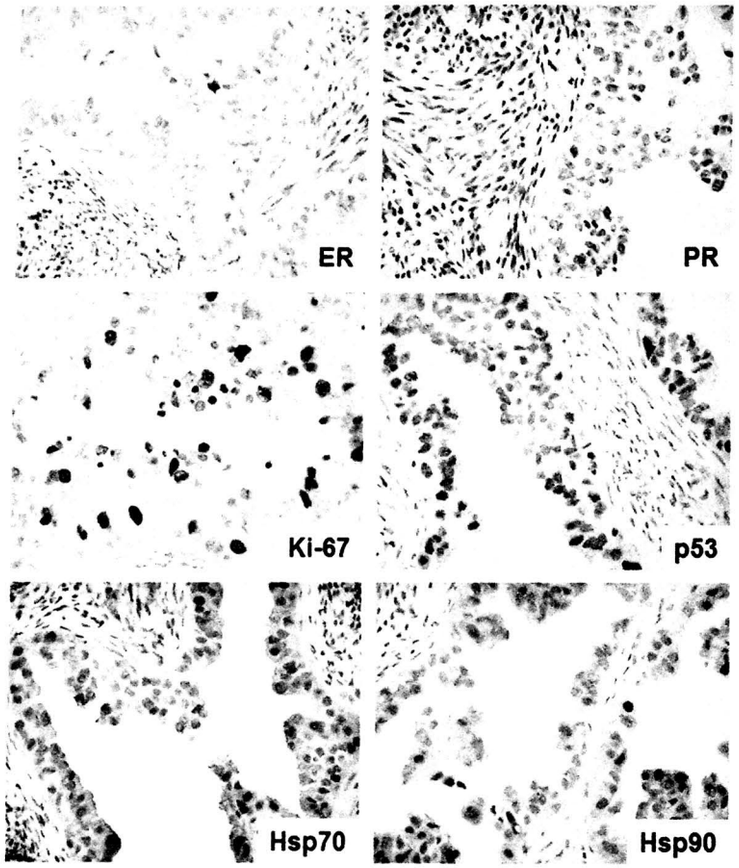

Figure 4. Serous carcinoma: negative expression of ER and PR, a pronounced expression of Ki-67 and p53, a pronounced nuclear-cytoplasmic expression of Hsp70 and Hsp90. Expression was evaluated exclusively in the epithelial component of the tissue. Immunohistochemical study of ER, PR, Ki-67, p53, Hsp70, and Hsp90. Magnification x400.

sensitivity to sex hormones and chaperone activity ($p > 0.05$). Instead, there was an increase of the Hsp70 and Hsp90 expression together with the intensification of cells' proliferative activity and the appearance of the number of p53-positive cells ($p < 0.05$).

Discussion. Endometrial carcinomas are a common pathology in women, the course of which depends on several prognostic factors [1, 2]. Like most other cancers of the reproductive system, their progression and sensitivity to therapy are determined by morphological and molecular genetic features of tumor tissue [16, 17]. Among them, sensitivity to antihormonal treatment (ER and PR expression) and proliferative-apoptotic activity of cells (Ki-67 and p53 expression) are the most proven prognostic markers [16, 18, 19].

Our study is devoted to studying the expression of Hsp70 and Hsp90 in the tissue of different endometrial carcinoma types (EC, SC, and CCC) with the establishment of their predictive value. Similar to the previously obtained results [5,10], we found both chaperones' expression throughout the menstrual cycle. Neoplastic transformation and anaplasia of tumor cells were accompanied by the intensification of Hsp70 and Hsp90 expression. Despite the proven synergy of chaperones and receptors for female sex hormones [12,13], we did not find a correlation between their expression. The main evidence of their influence on the endometrial cells' functioning was the Hsp70 and Hsp90 monotonous expression in different phases of the menstrual cycle, characterized by pronounced variability of the ER and PR expression. Intense chaperone expression in highly aggressive endometrial carcinomas (high-grade EC, SC, and CCC), which have low ER and PR expression, is thought to be more related to cancer cell anaplasia than to variability in female sex hormone receptor expression.

Increased Hsp70 and Hsp90 expression in endometrial carcinoma tissue was accompanied by the intensification of cell proliferative activity (number of Ki-67-positive cells) and synthesis of mutant p53. It proves their participation in modulating cell division and avoidance of apoptosis [5,6]. Their pronounced

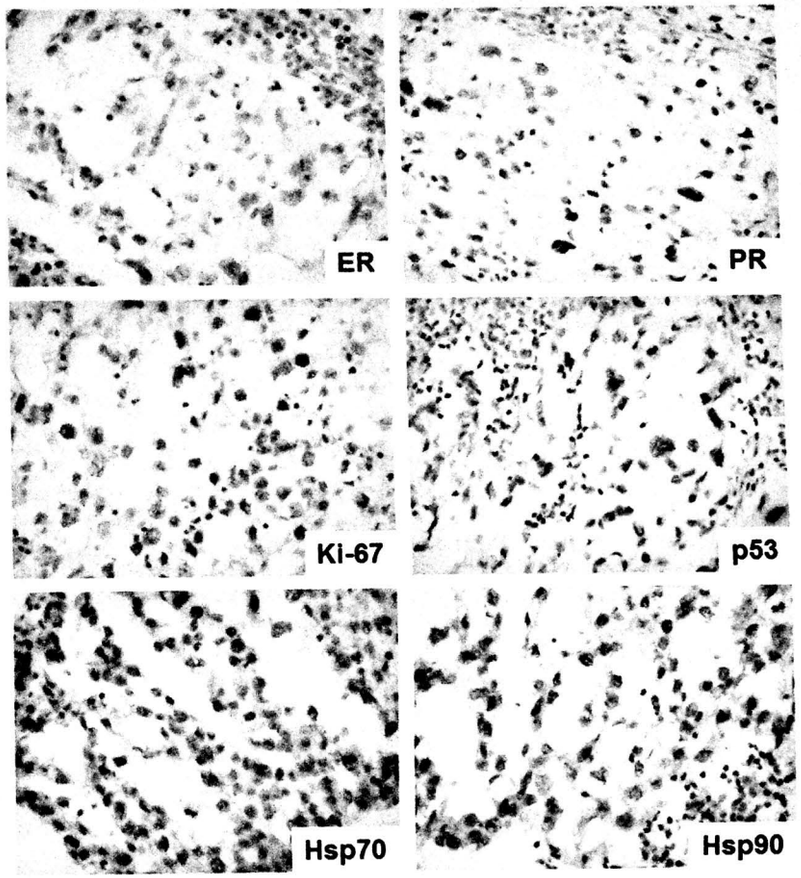

Figure 5. Clear-cell carcinoma: negative expression of ER and PR, a pronounced expression of Ki-67 and p53, a pronounced nuclear-cytoplasmic expression of Hsp70 and Hsp90. Expression was evaluated exclusively in the epithelial component of the tissue. Immunohistochemical study of ER, PR, Ki-67, p53, Hsp70, and Hsp90. Magnification x400.

overexpression in the nuclei of tumor cells may indicate that Hsp70 and Hsp90 are involved in the violation of apoptosis and cell division controls.

Our data has some inconsistencies with previous study results, which revealed inhibition of chaperone activity during carcinoma dedifferentiation [10], as well as the favorable prognostic value of Hsp70 and Hsp90 expression [6,14]. On one hand, this may be due to these proteins' unique properties depending on the topography of the tumors. On the other hand, the difference may depend on the group formation of the testing material, the reagents used, and the peculiarities of interpreting the obtained research results. All this encourages us to pursue further research of these protein properties. Confirmation of the Hsp70 and Hsp90 generation dependent [9] was the correlation between their expressions in the endometrial carcinoma tissues.

Based on this, Hsp70 and Hsp90 are involved in the normal endometrium's functioning and in the progression of endometrial carcinoma. Their prooncogenic effect leads to proliferative activity, increase of tumor cells, avoidance of apoptosis, and carcinoma dedifferentiation. This argues their determination in endometrial carcinoma tissue. Finally, differences in the interpretation of the results suggest using computerized equipment and intelligent programs for score standardization of immunohistochemical results [20]. It is hoped that this study will stimulate further investigations in this field.

Conclusions

In our study we have found the Hsp70 and Hsp90 involvement in the endometrial carcinoma progression. Their increased expression in tumoral cells correlates with proliferative activity intensification, p53 expression, and cell anaplasia. The Hsp70 and Hsp90 simultaneous and unidirectional activation in tumor tissue does not depend on the ER and PR expression. The variability of Hsp70 and Hsp90 expression in endometrial carcinomas highlights the importance of adding them to diagnostic panels with subsequent treatment personification.

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Ethical approval

The Bioethics Commission of the Medical Institute of the Sumy State University approved the protocol for this study (№ 4/6 of 16/06/2018).

Conflict of interest

The authors declare that they have no competing interests.

Informed Consent

Written informed consent was obtained from patients who participated in this study.

References

1. Kurman R.J., Carcangiu M.L., Herrington C.S., Young R.H. (Eds.): WHO Classification of Tumours of Female Reproductive Organs. IARC: Lyon 2014. 307 p.
2. Romaniuk A., Lyndin M., Smiyanov V. et al. Primary multiple tumor with affection of the thyroid gland, uterus, urinary bladder, mammary gland and other organs // Pathol Res Pract. 2017 May;213(5):574-9. DOI: 10.1016/j.prp.2017.01.003.
3. Yun C.W., Kim H.J., Lim J.H., Lee S.H. Heat Shock Proteins: Agents of Cancer Development and Therapeutic Targets in Anti-Cancer Therapy // Cells. 2019;9(1):60. DOI: 10.3390/cells9010060.
4. Sauvage F., Messaoudi S., Fattal E. et al. Heat shock proteins and cancer: How can nanomedicine be harnessed? // J. Control. Release. 2017;248:133-43. DOI: 10.1016/j.jconrel.2017.01.013.
5. Tabibzadeh S., Broome J. Heat shock proteins in human endometrium throughout the menstrual cycle // Infect Dis Obstet Gynecol. 1999;7(1-2):5-9. DOI: 10.1155/S1064744999000022
6. Ciocca D.R., Calderwood S.K. Heat shock proteins in cancer: diagnostic, prognostic, predictive, and treatment implications // Cell Stress Chaperones. 2005;10(2):86-103. DOI: 10.1379/csc-99r.1
7. Calderwood S.K., Gong J. Heat Shock Proteins Promote Cancer: It's a Protection Racket // Trends Biochem. Sci. 2016;41:311-23. DOI: 10.1016/j.tibs.2016.01.003.
8. Jagadish N., Agarwal S., Gupta N., Fatima R., Devi S., Kumar V., Suri V., Kumar R., Suri V., Sadasukhi T.C., et al. Heat shock protein 70-2 (HSP70-2) overexpression in breast cancer // J Exp Clin Cancer Res. 2016;35(1):150. DOI: 10.1186/s13046-016-0425-9

9. Noordhuis P., Holwerda U., Van der Wilt C.L., et al. 5-Fluorouracil incorporation into RNA and DNA in relation to thymidylate synthase inhibition of human colorectal cancers // Ann. Oncol. 2004;15:1025-32. DOI: 10.1093/annonc/mdh264
10. Wataba K., Saito T., Fukunaka K. et al. Over-expression of heat shock proteins in carcinogenic endometrium // Int J Cancer. 2001 Feb 15;91(4):448-56. DOI: 10.1002/1097-0215(200002)9999:9999.
11. Neuer A., Spandorfer S.D., Giraldo P. et al. The role of heat shock proteins in reproduction // Hum Reprod Update. 2000;6(2):149-59. DOI: 10.1093/humupd/6.2.149.
12. Spears P.A., Barnes J.A. HSP70 enhances MCF-7 cell growth and estrogen receptor activity // Proc 1st Int Cong Stress Responses Biol Med Quebec, 2003, September 10-14. pp. 73.
13. Nanbu K., Konishi I., Komatsu T. et al. Expression of heat shock proteins HSP70 and HSP90 in endometrial carcinomas. Correlation with clinicopathology, sex steroid receptor status, and p53 protein expression // Cancer. 1996;77(2):330-8.
14. Nanbu K., Konishi I., Mandai M. et al. Prognostic significance of heat shock proteins HSP70 and HSP90 in endometrial carcinomas // Cancer Detection and Prevention. 1998;22(6):549-55. DOI: 10.1046/j.1525-1500.1998.00069.x.
15. Romanjuk A., Lyndin M., Moskalenko R., Gortinskaya O., Lyndina Y. The Role of Heavy Metal Salts in Pathological Biomineralization of Breast Cancer Tissue // Adv Clin Exp Med. 2016;25(5):907-910. doi:10.17219/acem/34472
16. Hyriavenko N., Lyndin M., Sikora K. et al. Serous Adenocarcinoma of Fallopian Tubes: Histological and Immunohistochemical Aspects // J Pathol Transl Med. 2019;53(4):236-43. doi: 10.4132/jptm.2019.03.21
17. Lytvynenko M., Shkolnikov V., Bocharova T. et al. Peculiarities of proliferative activity of cervical squamous cancer in hiv infection // Georgian Med News. 2017 Sep;(270):10-5.
18. Romaniuk A., Lyndin M., Moskalenko R. et al. Pathogenetic mechanisms of heavy metals effect on proapoptotic and proliferative potential of breast cancer // Interv Med Appl Sci. 2015;7(2):63-8. DOI: 10.1556/1646.7.2015.2.4
19. Vynnychenko I.O., Pryvalova A.O., Vynnychenko O.I., Lyndin M.S., Sikora V.V., Romaniuk A.M. PIK3CA-mutant circulating tumor DNA in patients with breast cancer // Azerbaijan Medical Journal. 2020;3:79–88. DOI: 10.34921/amj.2020.3.010
20. Gargin V., Radutny R., Titova G., Bibik D., Kirichenko A., Bazhenov O. Application of the computer vision system for evaluation of pathomorphological images. 2020 IEEE 40th International Conference on Electronics and Nanotechnology, ELNANO 2020 - Proceedings; 2020:469-473 DOI: 10.1109/ELNANO50318.2020.9088898.

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РОЛЬ БЕЛКОВ HSP70 И HSP90 В ПРОГРЕССИРОВАНИИ ЭНДОМЕТРИАЛЬНЫХ КАРЦИНОМ

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Резюме. Проведено исследование с целью определения роли белков теплового шока (Hsp) 70 и Hsp90 в развитии карциномы эндометрия (эндометриоидная карцинома эндометрия, серозная карцинома эндометрия, светлоклеточная карцинома эндометрия) и их связи с рецепторами эстрогена и прогестерона, активности пролиферации и апоптоза.

Были использованы 40 образцов карциномы эндометрия (20 случаев эндометриоидных карцином, 10 – серозных и светлоклеточных карцином) для иммуногистохимического исследования HSP70, HSP90, ER, PR, Ki-67 и p53. Нормальные ткани эндометрия (n = 10) были взяты у женщин, страдающих лейомиомой матки.

Экспрессия Hsp70 и Hsp90 была представлена во всех случаях как нормальной, так и опухолевой ткани эндометрия. Неопластическая трансформация, дифференцировка опухоли и усиление анаплазии раковых клеток сопровождаются ростом интенсивности экспрессии Hsp70 и Hsp90, количества рецептор-положительных клеток и преобладанием ядерного пат-

терна над цитоплазматическим ($p < 0,05$). Их повышенная экспрессия в опухолевых клетках коррелирует с усилением пролиферативной активности и экспрессией p53 ($p < 0,05$). Одновременная и однонаправленная активация Hsp70 и Hsp90 в опухолевой ткани не зависит от экспрессии ER и PR.

Таким образом, результаты демонстрируют участие Hsp70 и Hsp90 в прогрессировании карциномы эндометрия. Их повышенная экспрессия в опухолевых клетках коррелирует с усилением пролиферативной активности, экспрессией p53 и анаплазией клеток. Вариабельность экспрессии Hsp70 и Hsp90 в карциномах эндометрия подчеркивает важность добавления их в диагностические панели с последующей персонификацией лечения.

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