

the cavity is greater than the flame stabilization in the combustion chamber, which is related to the power of the igniter discharge and the flow field environment inside the cavity . Experimental studies of the characteristics of detonation engines are relevant and involve the creation of a specialized laboratory and fire test stands for the rapid introduction of the latest technologies in the rocket and space industry.

REFERENCES

1. Chen, Y.; Wang, S.; Liu, W. Data-Driven Transition Models for Aeronautical Flows with a High-Order Numerical Method. *Aerospace* 2022, 9, 578. <https://doi.org/10.3390/aerospace9100578>
2. Curran, D.; Wheatley V.; Smart M. High Mach Number Operation of Accelerator Scramjet Engine. Published by the American Institute of Aeronautics and Astronautics, Inc., with permission. Published Online: 2 Jan 2023 <https://doi.org/10.2514/1.A35511>
3. Sosnovska O. V.; Zolotko O. E.; Zolotko O. V.; Stoliarchuk V. V. Ejector detonation engine based on ecologically clean fuel components. *Aerospace technique and technology*. 2021-08-27/ doi: 10.32620/akt.2021.4.03
4. Tian, S.; Duan, Y.; Chen, H. Numerical Investigation on Aerodynamic Characteristics of an Active Jets-Matrix Serving as Pitch Control Surface. *Aerospace* 2022, 9, 575. <https://doi.org/10.3390/aerospace9100575>

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MODERN CONCEPTS

ON THE PATHOGENESIS OF UTERINE FIBROIDS

Uterine fibroids, also often referred to as leiomyomas, are benign monoclonal tumors that develop from smooth muscle cells in the myometrium. This is the most common neoplasm in women of reproductive age and is diagnosed in 30-35% of patients [1]. In 30% of cases, uterine fibroids become symptomatic, which is manifested by pelvic pain, infertility, poor reproductive prognosis and uterine bleeding, often leading to anemia. The development of symptoms in this pathology depends on the location and size of the tumor, but most often a vivid clinical picture is observed with atypical localizations of large nodes. The most common companion of uterine fibroids is pain syndrome, as a rule, it is manifested by secondary dysmenorrhea, cramping pains with a submucosal location of the node, aching pains with the rapid growth of the node, its large size, also with

the interligamentous location of the tumor, compression of neighboring organs, degenerative changes in the node and concomitant inflammatory diseases of the genitals. As a result of the development of the above symptoms, uterine fibroids, according to various sources, become the number one reason for hysterectomy [2].

Certain factors have been proven to contribute to the formation of uterine fibroids, such as early menarche, no history of pregnancy or childbirth, late reproductive age, menstrual irregularities (chronic anovulation, dysmenorrhea), caffeine and alcohol use, obesity, and high blood pressure.[2].

The widespread prevalence of uterine fibroids in women inevitably raises the question of the pathogenesis of the disease for scientists, but, despite the huge number of works devoted to this topic, there are many unexplored aspects.

M. Wolanska indicates the ability of growth factors to modulate the action of estrogens, which in turn stimulate their synthesis [3]. Thus, constant self-stimulating proliferation and hyperplasia associated with the circulation of sex hormones and the synthesis of growth factors can presumably take place in the uterine myoma.

Blood circulation also plays an important role in the development of fibroids. N. Takahashi et al. investigated the blood flow in the uterine artery in women with and without fibroids, as a result of which an increase in blood flow in the uterine artery in women diagnosed with uterine myoma was revealed. Studies of the ASL (arterial spin labeling) signal determined that the myomatous node is capable of causing an imbalance in the distribution of blood in the myometrium. Increased angiogenesis is associated with increased expression of growth factors such as VEGF, bFGF and PDGF [4].

The question of the role of genetic predisposition to uterine myoma is still open. The presence of familial forms of fibroids, the revealed relationship between the development of pathology and race certainly suggests the presence of certain genetic defects that contribute to the development of the disease. However, various chromosomal aberrations are found in 40% of tumors, which requires further study of this issue [2]. There is also a version that the mutation of the MED12 gene responsible for the activation of the P-cadherin gene plays an important role in

the pathogenesis of uterine fibroids, according to some reports, it leads to the development of uterine fibroids.

Recently, the theory of microRNA involvement in the pathogenesis of uterine fibroids has become increasingly popular. It is assumed that miRNA affects the regulation of the cell cycle, apoptosis, and cell differentiation. It was found that microRNA-21 controls the expression of the transforming growth factor-P type 2 receptor (the key profibrotic cytokine that causes cell hypertrophy, disrupts the exchange of extracellular matrix components and affects angiogenesis). J.B. Fitzgerald et al. proved that an increase in miRNA-21 affects the reduction of apoptosis, since the study was able to detect an increase in the cleavage of caspase-3, which is a marker of apoptosis, with a decrease in the level of miRNA-21 [5].

The primary cell from which uterine fibroids subsequently develop can probably be a mesenchymal cell or a smooth muscle cell of the myometrium.

Mas et al. indicate the presence in the myoma of SP cells (side population, an additional population of stem cells capable of differentiating into myoblasts) with SC (stem cells, stem cells) – characteristics of tumor-forming cells. The proportion of SP in the entire leiomyoma fraction was $0.63 \pm 0.21\%$. It does not depend on the age of the patients, the state of fertility, the location of the fibroid and its size. Molecular characterization of these cells has shown that they are not yet lineage-bound, as they lack typical muscle markers (smutelin and calponin) and hormone receptors (ESR1, estrogen receptor 1 and PR, progesterone receptor). It is hypothesized that tumor growth may be the result of an interaction between cancer stem cells and tumor-initiating cells and their microenvironment. These cells are organized like normal tissues, with a small self-renewing population of stem cells generating a large population of proliferating cells that is distinct from the rest. Thus, they are initiated by a small subset of tumor cells that are ultimately responsible for their formation and growth.[6].

Stem cells, of course, are found not only in pathologically altered fibroid tissue, but also in healthy myometrium. M. Orciani et al. also explains the development

of uterine fibroids by deregulation of mesenchymal stem cells. Thus, the development of fibroids may be the result of impaired function, proliferation and differentiation of undifferentiated myometrial cells, which are under the influence of ovarian hormones. The authors also point out the possible influence of the inflammatory process on the dysregulation of progenitor cells [7].

Despite the abundance of theories and hypotheses on the pathogenesis of uterine fibroids, to date there is no complete understanding of the causes of the development of this pathology. It is worth noting the need for further research in order to study the processes leading to the development of fibroids, since their understanding could largely improve the tactics of treating patients and, possibly, allow the development of preventive measures to prevent the development of fibroids.

REFERENCES

1. Friederike Hoellen, Georg Griesinger, Michael K Bohlmann. Therapeutic drugs in the treatment of symptomatic uterine fibroids <https://pubmed.ncbi.nlm.nih.gov/23914973/>
2. Ministry of Health Protection of Ukraine. Standards of medical assistance "Uterine leiomyoma".
3. Wolanska M, Malkowski A, Romanowicz L, Bankowski E. Does vascular endothelial growth factor participate in uterine myoma growth stimulation? *Eur J Obstet Gynecol Reprod Biol.* 2012;164(1):93-97. <https://doi.org/10.1016/j.ejogrb.2012.05.021>.
4. Takahashi N, Yoshino O, Hiraike O, et al. The assessment of myometrium perfusion in patients with uterine fibroid by arterial spin labeling MRI. *Springerplus.* 2016;5(1):1907. <https://doi.org/10.1186/s40064-016-3596-0>.
5. Fitzgerald JB, Chennathukuzhi V, Koohestani F, et al. Role of microRNA-21 and programmed cell death 4 in the pathogenesis of human uterine leiomyomas. *Fertil Steril.* 2012;98(3):726-734 e722. <https://doi.org/10.1016/j.fertnstert.2012.05.040>.
6. Mas A, Cervello I, Gil-Sanchis C, et al. Identification and characterization of the human leiomyoma side population as putative tumor-initiating cells. *Fertil Steril.* 2012;98(3):741-751.e746. <https://doi.org/10.1016/j.fertnstert.2012.04.044>.
7. Orciani M, Caffarini M, Biagini A, et al. Chronic inflammation may enhance leiomyoma development by the involvement of progenitor cells. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5971255/>