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Ionizing radiation-induced epigenetic modifications and transgenerational effects

Abstract. *Nowadays a number of nations are exploring differences in gene expression resulting from changes in DNA methylation and modification of chromatin structure in response to external stimuli, such as radiation. It has been also well known that Ionizing radiation affects variety processes in exposed cells, in particular, cause changes in gene expression, mitochondria metabolic activity, chromosomal instability, apoptotic cell death and other changes at the molecular level. The point of view of the transgenerational nature of genomic instability suggests the possible involvement of epigenetic mechanisms. Kazakhstan has the potential to be exposed to a variety of hazardous materials, including radon, a radioactive gas that naturally occurs as a result of the indirect decay of uranium. It is also important to indicate that the Republic of Kazakhstan is considered the leader in terms of large reserves of uranium ores. Radioactive contamination is considered to be an important point that affects both the surrounding environment and human health. According to the World Health Organization, chronic exposure to radon and its decay products is the number one cause of lung cancer in non-smokers. All of the above facts prove the long-term pollution of the atmosphere by radiation has consequences for the health of the nation. Taking into account the importance of radon as a risk factor for lung cancer, this review focuses on discussion of possible radiation-induced alterations.*
Keywords: *radiation, radon, epigenetics, miRNA.*

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Radiation, types of ionizing radiation, physical properties

Radiation is the energy that has the ability to come from unstable atoms undergoing radioactive decay. Radiation propagates from the source in the form of energy waves or charged particles. Humans are exposed to ionizing radiation in every walk of life owing to its diverse use, from medical diagnostics to industrial applications. Ionizing radiation is a component of our environment and an important tool in medical treatment. There are two types of radiation such as non-ionizing radiation and ionizing radiation.

Non-ionizing radiation is known for having enough energy for the atoms in a molecule to move or vibrate, but not enough to remove electrons from the atoms. Examples of this kind of radiation are radio waves, visible light, and microwaves, and ultrasound waves, and it is also used in magnetic resonance imaging. These forms of NIR are present in our daily lives. Ultrasound waves and magnetic resonance imaging are often used in medical examinations.

Ionizing radiation has so much energy it can knock electrons out of atoms, a process known as ionization. Ionizing radiation can affect the atoms of living creatures, because of which it poses a threat to well-being, damaging tissues, and DNA in the genes. Ionizing radiation comes from X-ray machines, galactic particles from space, and radioactive constituents. Radioactive constituents emit ionizing radiation when their atoms undergo radioactive decay.

Radioactive decay is the release of energy in the form of ionizing radiation. The ionizing radiation emitted can include alpha particles, beta particles, and gamma rays. Radioactive decay occurs in unstable atoms called radionuclides.

Ionizing radiation can be categorized as either electromagnetic or particulate energy. Electromagnetic energy consists of γ-rays and X-rays, which can penetrate human tissues; thus, exposure to γ-rays and X-rays can cause serious damage to organs. Particulate energy includes alpha

particles and beta particles, which can only penetrate a few millimeters of skin. This lack of penetrating power means that these particles do not cause significant damage to organisms, but they may act as carcinogens or have other adverse health effects when injected or inhaled.

The health effects of alpha particles are unimaginably dependent on how the person is influenced. Alpha particles do not have enough energy to get through the outer layer of the skin, as a result of which the influence on the body from the outside is not considered a serious problem. However, from the inside of the body, they have every chance of being quite harmful. If alpha emitters are inhaled, swallowed, or enter the body through a cut, alpha particles have every chance of destroying organ tissues. The damage from these large, heavy alpha particles makes them more dangerous than other forms of radiation. The ionizations they cause are very close to each other - they can release all their energy in several cells. This leads to more severe damage to cells and DNA.

Beta particles have greater penetrating power than alpha particles but cause less damage to living tissues and DNA because the ionization they produce spreads more extensively. They travel further than alpha particles, but it is possible to stop their penetration with a layer of clothing or a thin layer of a material such as aluminum. Some beta particles are ready to seep through the skin and cause damage, such as skin burns. However, as with alpha-emitters, beta-emitters are most hazardous when they are inhaled or swallowed.

Gamma rays are similar to visible light but have much higher energy. Gamma rays are often emitted in conjunction with alpha or beta particles during radioactive decay. Gamma rays pose a radiation threat to the entire body. They have every chance of simply seeping through obstacles that can slow down alpha and beta particles, such as skin and clothes.

Ionizing radiation is now generally accepted as a severe DNA-damaging agent, which can lead to severe diseases such as cancer. It has been also well known that the effects of Ionizing radiation on genomic instability have a transgenerational nature. Thus, they are the precursors of tumorigenesis and genetic and epigenetic effects.

One of the most hazard radioactive particles in the environment is radon, which affects human internal organs. Radon (Rn-222) is a natural radioactive noble gas that originates from the decay series of uranium-238, which can be found in soil, water, outdoor, and indoor air. Radon exposure accounts for over 50% of the effective annual dose of natural radioactivity. Recently worldwide, social interest in radon exposure and its health effects have increased greatly. Environmental exposure to radon is a risk factor for respiratory diseases. Also, it is important to note that the Republic of Kazakhstan is a leader in the world reserves of uranium ores, producing the largest share of uranium from mines (41%), followed by Canada (13%), Australia (12%), USA, France, Germany, and Spain. In these countries, there is a high concentration of radon in the atmosphere and water [1, 2].

A recent estimate put the radon contribution at 14% of total lung cancer deaths. The main source of radon in the air and living quarters is its passive diffusion from the soil. Radon migrates out of soil and rock into the surrounding air, resulting in accumulation in poorly ventilated or closed areas. Such areas represent the primary environments in which humans are exposed to radioactivity from radon [3].

Radon emits multiple high linear energy transfer (LET) alpha particles upon radioactive decay and has been found to be carcinogenic to humans by the International Agency for Research on Cancer. The high-linear energy transfer of α-particles emitted by radon and radon decay products can directly attack genomic DNA and cause mainly double-strand breaks in DNA. In comparison with the damaging effects of β-, and γ- radiation, alpha particles cause around 40 times more severe radiation damage. The decay of α-particles results in the ejection of electrons from water, generating several oxidative reactive species leading to cellular damage by hydroxyl radical attack [2, 4]. Currently, residential radon exposure is considered the second highest cause of lung cancer and the leading cause among nonsmokers. Exposure to radon leads to the inconstancy of the genome, in fact, which causes the accumulation of numerous genetic changes and leads to the

development of cancer. Radon is an environmental toxin that has the ability to increase the risk of lung cancer with long-term exposure. The highest values of radon are found in the northern and eastern regions of Kazakhstan due to natural sources of radiation and long-term and large-scale uranium mining.

Radon particles can damage cellular components by two mechanisms: LET and the oxidation of cell components by reactive oxygen species (ROS). As they pass through the cell, the movement speed of alpha particles decreases, resulting in more energy releasing per unit of track length, which leads to the damage of cellular components. The path of the particle through the nucleus of the cell crosses many strands of DNA, and the energy released during these breaks the phosphodiester bond, resulting in the formation of double-stranded DNA breaks (DSBs) [5]. This leads to the most cytotoxic lesions caused by radon, and, in the case of defects in the work of the reparative systems, the formation of such breaks can lead to chromosomal instability [6]. Chromosomal instability is not only one of the causes of carcinogenesis but also contributes to tumor adaptation to cytotoxic anticancer drugs 7, 8]. The epigenetic basis of lung cancer is related primarily to changes in the profile of miRNA. miRNAs are a class of small single-stranded non-protein-coding RNAs that play important roles in different cellular processes including cell development and proliferation, differentiation, growth control, and apoptosis [2, 9-11]. In connection with exposure to radon, it is possible to observe the change in microRNA profiles, using it as a tool for early cancer diagnosis.

There is enough research evidence about the role of mitochondria in the cellular response. Radiation changes the structure and function of mitochondria developing oxidative stress. Mitochondria constitute a major intracellular source of reactive species, as they generate almost 90% of the total number of cellular ROS [12]. High intra-mitochondrial ROS levels can damage the mitochondrial DNA, causing global DNA hypomethylation, by decreasing the activity of DNMTs and these changes are transmitted to the progeny of the irradiated cells [13]. These observations suggest that mitochondrial dysfunction can cause oxidative DNA damage and contributes to an altered epigenetic landscape to perpetuate radiation-induced instability [14]. Thus, the mutated mtDNA (or its absence) may affect the expression level of p53 and, in consequence, the expression profile of genes that are under the transcriptional control of p53. Furthermore, the key elements of the cellular response to ionizing radiation, and induction of p53 activity are missing in the absence of mitochondrial respiration. Detailed molecular mechanisms remain to be discovered. Thus, there is no doubt that mitochondria play a key role in cellular responses to various types of ionizing radiation, including the development of cellular aging.

According to *Liu* et al. dates examined mitochondrial damage and the Warburg effect in malignantly transformed human bronchial epithelial cells following exposure to radon. Based on these findings, it has been suggested that mitochondrial damage and SDHA-mediated aerobic glycolysis may play a crucial role in cell malignant transformation induced by radon. The Warburg effect is a well-known metabolic hallmark of cancer. Studies have shown that long-term exposure to radon in human bronchial epithelial cells indicated an obvious Warburg effect, and we identified that the p53-mediated energy signaling pathway plays a crucial role in radon-induced malignant cell transformation [15].

Taking into account the hazardous effects of radon, causing lung cancer, which is the leading cause of death in the world, it is important to make research in this area.

Epigenetics. Main mechanisms: histone variants, miRNA, and DNA methylation

Epigenetic events are known to regulate gene activity and expression during development and differentiation. In particular, epigenetic mechanisms regulate the gene expression in our body's cells to create all the different cell types, although they have the same genome. However, they also affect gene expression in response to environmental stimuli, including ionizing radiation [16]. The main epigenetic changes currently considered are DNA methylation, histone modification, and modulation of non-

coding RNAs (ncRNAs) [17]. It is generally assumed that the accumulation of genetic modifications favors the development of cancer. While this concept is the basis of our knowledge of cancer progression, it cannot explain the heterogeneity of tumor cell growth, invasion, or resistance to therapies. The important role that epigenetic phenomena play in carcinogenesis is increasingly recognized.

Epigenetics is one of the most quickly growing fields of biomedical research, as well as one of the most intriguing and promising in terms of improving our understanding of disease etiologies and seeking new treatment techniques. Recent landmark events in this area include the characterization of human DNA methylome with single nucleotide resolution, the discovery of CpG island coasts, the identification of new histone variants and modifications, and the development of maps of the whole genome of the positions of the nucleosomes. Much of our better understanding is the result of technological breakthroughs that have made it possible to conduct large-scale epigenomic studies. These new methodologies have enabled ever finer mapping of the epigenetic marks, such as DNA methylation, histone modifications, and nucleosome positioning that are critical for regulating the expression of both genes and noncoding RNAs. Epigenetic processes, i.e., alterations to biological information without changes in the DNA sequences that are mitotically or meiotically heritable, go beyond DNA-stored information and are essential for packaging and interpretation of the genome [18].

DNA methylation is a covalent chemical modification resulting in addition of a methyl (CH3) group at the carbon 5 position of the cytosine ring of CpG dinucleotides. CpG sites are concentrated either in repetitive sequences or CpG islands in promoter regions. Methylation of CpG islands naturally takes place during X chromosome inactivation and imprinting, though the majority of CpG islands remain unmethylated during development and differentiation. Extensive changes in DNA methylation during the processes of differentiation are known to take place at CpG island shores, regions of comparatively low CpG density close to CpG islands [19].

Post-translational histone modifications identified so far include acetylation, phosphorylation, methylation, and monoubiquitination. Histone acetylation occurs at specific lysine residues in the histone tails and is a reversible covalent transformation. This modification can neutralize the positive charge of the targeted lysine, weakening the histone-DNA [20] or nucleosome interactions and, therefore, causing conformational changes leading to an open chromatin structure [21]. Histone acetylation is almost always associated with transcriptional activation [22] and while the majority of acetylation sites are present within the N-terminal histone tail, which is more accessible for transformation, acetylation in the H3 core domain at lysine 56 (H3K56ac) has yet to be reported [23].

Histone methylation is a reversible modification mainly occurring on the side chains of both lysines and arginines [24, 25]. Up to three methyl groups can be added to a single lysine residue, creating four different methyl modifications in total: unmethylated, mono-, di-, or trimethylated states. That is why methylation is unique among all post-translational modifications of histones. Apart from this, the remains of arginine have every chance of being subjected to both monomethylation and dimethylation, while the latter contains a symmetrical or asymmetric configuration [24].

Histone phosphorylation, like other histone modifications, is a highly dynamic process whose structure is characterized by the addition of a phosphate group from ATP to the hydroxyl group of the target amino acid side chain of several and various residues in histone tails. The addition of a phosphate group and, consequently, a negative charge can modify the chromatin structure and thus affect the interaction between transcription factors and other chromatin components [26, 27]. Histone phosphorylation takes place on serine (S), tyrosine (Y), and threonine (T), with the vast majority of histone phosphorylation sites being found within the N-terminal tails and only a very few examples, such as H3Y41, are found within the histone core [26, 28].

Amongst multiple post-translational modifications, protein ubiquitination is a common and important process in cells [29, 30]. The diversity of ubiquitination types includes monoubiquitination, multiubiquitination, and polyubiquitination, each having different cellular functions [31]. Histone

ubiquitination occurs primarily in a mono-ubiquitinated form and correlates with active and open chromatin. Although depending on the genomic structure histone ubiquitination could be associated with both transcriptional activation and silencing [32, 33]. Monoubiquitination is involved in DNA repair, gene expression, and receptor endocytosis. Furthermore, a role of monoubiquitination at histone H2A linked to DNA repair mechanism has been reported [34]. Polyubiquitination of Ub-K48 targets a protein that needs to be degraded. Genetic and epigenetic aberrations, such as mutation, amplification, and deletion, can be the common causes of dysregulated ubiquitination and deubiquitination in cancer cells [35].

One of the important factors regulating the functioning of eukaryotic cells at the nucleosome level is the replacement of histones by their variants. There are two types of histones: canonical and variant histones. Variant histone genes are expressed throughout the cell cycle while canonical histone genes are exclusively expressed in the S phase [36]. Known histone variants belong to the H1, H2A, and H3 histone families [37, 38]. Histone variants contain a unique ability to regulate key cellular and developmental processes, and, when deregulated, may contribute to cancer initiation and progression. Indeed, a growing body of evidence links histone variants to cancer biology. For example, the expression level of particular variants correlates with tumor malignancy in a number of different tumor types, and, thus, histone variants may be utilized as prognostic indicators in cancer (described below in detail) [39, 40].

Another important element is a miRNA which regulates gene expression affecting many cellular mechanisms. miRNAs have emerged as an interesting area of basic and translational biomedical study, owing to their influence on gene expression, robust presence in bodily tissues and fluids, and their potential utility as disease biomarkers [41, 42]. miRNAs primarily affect gene expression levels via targeting mRNA. Any changes in miRNA expression may affect the extent of target regulation, and thus influence cell homeostasis [43, 44]. Therefore, the relative levels of miRNA, and consequently mRNA, have a major role in carcinogenesis and other diseases. It is currently believed that miRNAs can make up somewhere in the region of 1–3% of the entire human genome [45, 46] and estimates of the number of miRNA targets show that they can play a role in the regulation of up to 30% of mammalian genes [47]. Consequently, miRNA have been shown to play central roles in developmental timing, hematopoietic cell differentiation, programmed cell death, and oncogenesis [48].

Although the main role of miRNAs is to perform post-transcriptional gene regulation, their control of other non-coding RNAs has reshaped our understanding of RNA biology. miRNAs have been found to interact with long non-coding RNAs (lncRNAs), circular RNA (circRNA) and pseudogenes to either induce miRNA suppression or increase cellular competition for miRNA binding sites [49, 50, 51]. MiRNA are involved in the regulation of important cellular processes, such as proliferation [52], cell death [53], angiogenesis [54], invasion and metastasis [55], a dysregulation that is a hallmark of cancer [56]. Thus, it is not surprising that abnormal miRNA expression has been demonstrated in many different cancers.

These examples show how indirect control of miRNAs via transcription factors, promoters and epigenetics has wider implications on miRNA expression, and the capacity to influence several cellular pathways, including those in cancer development [57].

Radiation-Induced Epigenetic Changes

Ionizing radiation can induce a broad spectrum of DNA changes such as: base damage, sugar damage, single strand breaks (SSBs), double strand breaks (DSBs), DNA–DNA and DNA–protein cross-links. Indeed, ionizing radiation is uniquely very efficient at inducing clustered DNA lesions [58]. At low doses, even the passage of a single particle can produce clustered DNA lesions [59]. The frequency and degree of clustering of DNA damage depend on radiation quality.

It is well known that ionizing radiation can cause DNA damage, both directly in DNA and indirectly via reactive chemical species generated around DNA [60], and that the spectrum of damage depends radiation quality [61]. Indirect DNA damage by water free radicals is the most common mechanism for low LET radiation, while direct DNA damage predominates for high LET [17]. These radicals are formed by the radiolysis of water, of which hydroxyl radicals are considered the most harmful. Under aerobic conditions, these free radicals are converted into ROS containing both free radicals and non-free radicals.

As mentioned before, the main mechanism of ionizing radiation is the development of oxidative stress. Oxidative stress also contributes to epigenetic changes by altering the action of ncRNAs, in particular miRNA. However, the interactions between ROS metabolism and miRNA levels appear to be complex. Oxidative stress is caused by various factors such as ionizing and UV radiation, chemicals present in the environment or food, and pathogens. Numerous reviews contain data characterizing the relationship between oxidative stress and carcinogenesis, as well as tumor progression. Therefore, it is of considerable interest to study post-exposure oxidative stress at the cellular level. It is associated with chronic oxidative stress in ionizing radiation-surviving cells and their progeny, and is thought to be a cellular mechanism that allows precancerous cells to acquire typical malignant features. Genomic instability is expressed as increased levels of chromosomal aberrations, mutations, cell death, and mitotic failure [13].

Mitochondria also appear to have an important role in radiation-induced global DNA hypomethylation. Dysfunction of mitochondria can affect epigenetic regulation [62]. As a rule, the role of mitochondria in the epigenetic response of a cell to radiation exposure is associated primarily with changes in the genomic DNA methylation profile.

Overall, these data indicate that low-LET radiation exposure results in global DNA hypomethylation. However, it is important to identify whether or not hypomethylation is uniformly distributed throughout the genome, and whether there is also specific locus hypermethylation, which is known to be associated with inactive chromatin state and in most cases with repressed gene expression activity [63, 64, 65]. Specific-gene hypermethylation often involves normally unmethylated CpG islands, and can be associated with transcriptional silencing of the corresponding gene. If it is a suppressor gene, its loss of function may be a key event contributing to the oncogenic process [66. 67, 68]. Indeed, some studies have shown a significant DNA hypermethylation of tumor suppressor genes in workers exposed to ionizing radiation [69, 70]. Furthermore, gene-specific DNA methylation alterations have been found in X-ray irradiated human breast cancer cells [71]. Interestingly, this differential methylation changes correlate with already known biological responses to radiation, such as those on cell cycle, DNA repair, and apoptosis.

Cell exposure to ionizing radiation results in a wide variety of histone modifications. A well-known radiation-induced histone modification is histone H2AX phosphorylation, which is crucially important for maintaining the stability of the genome and repairing DNA double-strand breaks. Phosphorylation of this histone at serine 139 (γ-H2AX) is an early cellular response to ionizing radiation and is used as a measure of DSBs [72, 73]. In an in vivo murine model, low-dose X-ray irradiation resulted in decreased tri-methylation of histone H4 in the thymus accompanied by an overall reduction in chromatin compactness, a significant increase in global DNA hypomethylation as well as an accumulation of DNA damage and was associated to a reduced expression of DNMTs [74]. Similar histone modifications were found in human breast cancers [75]. These findings demonstrate that radiation-induced changes in DNA methylation and histone modifications result in overall GI. Furthermore, it has been shown that chromatin modification by histone acetylation is also crucial for DNA repair [76], and that chromatin acetylation is involved in several important steps such as chromatin remodeling and tagging of DSBs, activation of repair regulators, cell cycle regulation, and apoptosis [77].

miRNAs regulate a variety of cellular processes, including those induced by the effects of radiation exposure. Several studies recognize miRNAs as biomarkers for assessing the degree of radiation contamination with radon. They are important regulators of various genes associated with the risk of lung cancer [8]. A number of studies have examined the general and specific effects of miRNA disruption in different cell types exposed to low-LET ionizing radiation [78]. miRNAs have been shown to be involved in the response of irradiated cultured human cells [79]. In particular, it was shown that ionizing radiation affects miRNA levels in human endothelial cells [80]. Overall, these studies revealed that the expression levels of several miRNAs change significantly upon irradiation and indicated a specific role of various miRNAs on cellular radiosensitivity [81].

We have researched that cf-mtDNA levels were significantly higher in patients with radon-induced lung cancer than in other study participants. There was a significant difference in the level of cf-mtDNA in the blood plasma of healthy subjects exposed to high doses of radon and not exposed. In addition, mtDNA copy number was higher in healthy individuals living in areas with high radon concentrations than in lung cancer patients who were not exposed to high doses of radon. In addition, the results of our previous studies indicate that the microRNA expression profile is significantly changed by exposure to alpha radiation in individuals living in areas with elevated radon levels [83].

Transgenerational epigenetic effects of ionizing radiation

The inherited change in gene expression induced by a prior stimulus such as ionizing radiation is often referred to as epigenetic memory. Epigenetic memory is a kind of "imprint" that maintains gene expression states across cell generations in the absence of changes in the DNA sequence and in the absence of the original stimulus. Epigenetic memory can be considered on different time scales: cellular and transcriptional memory (mitotic heritable) and transgenerational memory (meiotic heritable) [82]. In many cases, epigenetic changes have been shown to be stable and can lead to transgenerational hereditary changes. In plants and some animals like nematodes, transgenerational epigenetic inheritance is well documented and relatively common [84]. Numerous examples of transgenerational epigenetic effects have been reported, in which environmental exposures, including ionizing radiation, lead to heritable phenotypic changes that pass-through male, female and sometimes both germlines [85]. In mammals, epigenetic patterns are largely erased and then remodeled during germ cell development and early embryonic development (epigenetic reprogramming) [87, 88]. Radiation-induced transgenerational effects may involve radiation-induced genome instability.

Radiation-induced transgenerational effects belong to an epigenetic phenomenon that could not be defined as a transmission of altered phenotypes from the irradiated parents to their non-exposed offspring. The transgenerational effects of paternal exposure to ionizing radiation were also observed by studying other genetic endpoints. It was shown that paternal irradiation significantly increases the frequency of chromosome aberrations in their first-generation offspring.

Given that the majority of epigenetic marks in mammals, such as DNA methylation, are erased after fertilization, it would appear that changes in DNA methylation in the germline of irradiated males may not contribute to the phenomenon of transgenerational inheritance. According to the results of recent studies, the mechanisms of Accepted Manuscript epigenetic inheritance can be attributed to the non-coding RNAs. It was also shown that in mammals non-coding RNAs can be transmitted to maturing sperm by small extracellular vesicles epididymosomes. It has been shown that miRNA-containing extracellular vesicles are present in the blood of irradiated mice. It would therefore appear that extracellular vesicles can be trafficked from blood to sperm. Indeed, according to the results of a recent study, the miRNA spectrum in sperm of irradiated mice significantly differs from that in [88].

Conclusion

The observations in the study suggest that the environment affects the body without the involvement of genetic mechanisms. The study of the role of epigenetics in the basic biochemical processes of the organism greatly expands our understanding of the disease development. Currently, one of the topical subjects for studying the possibilities of preventing the development of diseases is the study of transgenerational effects, when not only genetic but also phenotypic adaptive mechanisms are transmitted through generations. The studied data indicate that the influence of environmental factors (bad habits, stress, overnutrition or malnutrition, intestinal microbiota and others) during early development may contribute to the epigenetic transgenerational inheritance of phenotypic variability. Epigenetic processes can alter gene expression, which can either increase susceptibility or promote disease tolerance in future generations. Epigenetic biomarkers could in the future be used as a diagnostic tool to assess whether a person has a specific susceptibility to disease or exposure to environmental toxins.

The study of ionizing radiation is a topical subject in the field of biomedicine, as it is the main cause of changes in the genome. Ionizing radiation affects the level of microRNA, which in turn regulates many cellular mechanisms. MiRNA in body fluids is stable and available for research. This makes them non-invasive biomarkers of particular interest. Circulating miRNAs will be used not only in the field of oncological diseases, but also in many other pathologies. Another breakthrough in science that we are currently exploring is the study of microRNAs in circulating vesicles, such as exosomes, which contain the microRNAs of the cell from which they originated. Isolation of exosomes is now available through a variety of isolation techniques and allows them to be studied as biomarkers based on their cellular origin. Thus, it is possible to analyze all the data on the use of miRNAs as biomarkers in biological fluids and consider the emerging prospects for circulating vesicular forms of miRNAs to assess the state of cells and tissues synthesizing them. Our study provides evidence for a possible role of cf mtDNA as a promising biomarker of lung cancer induced by exposure to high dose of radon.

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Иондаушы сәулеленуден туындаған эпигенетикалық модификациялар және трансгенерациялық әсерлер

Аңдатпа. Қазіргі уақытта бірқатар елдер ДНҚ метилденуі мен хроматин құрылымының сәулелену сияқты сыртқы тітіркендіргіштерге жауап берудегі өзгерістерден туындайтын ген экспрессиясындағы айырмашылықтарды зерттеуде. Сондай-ақ иондаушы сәулеленудің әсер етуші жасушалардағы әртүрлі процестерге әсер ететіні, атап айтқанда, гендердің экспрессиясының өзгеруіне, митохондриялардың метаболикалық белсенділігіне, хромосомалық тұрақсыздыққа, жасушалардың апоптозға ұшырауына және молекулалық деңгейде басқа өзгерістерге әкелетіні белгілі. Геномдық тұрақсыздықтың трансгенерациялық табиғатының көзқарасы эпигенетикалық механизмдердің ықтимал қатысуын болжайды. Қазақстан әртүрлі қауіпті материалдардың, соның ішінде уранның жанама ыдырауынан табиғи түрде пайда болатын радиоактивті газ – радонның әсеріне ұшырауы мүмкін. Сондай-ақ, Қазақстан Республикасы уран кендерінің үлкен қоры бойынша көшбасшы болып саналатынын атап өту маңызды. Радиоактивті ластану қоршаған ортаға да, адамның денсаулығына да әсер ететін маңызды фактор болып саналады. Дүниежүзілік денсаулық сақтау ұйымының мәліметі бойынша, радонның және оның ыдырау өнімдерінің созылмалы әсері темекі тартпайтын адамдарда өкпе ісігінің бірінші себебі болып табылады. Жоғарыда аталған фактілердің барлығы атмосфераның ұзақ уақыт бойы радиациямен ластануының халық денсаулығына зиянын тигізетінін дәлелдейді. Өкпенің қатерлі ісігінің қауіпті факторы ретінде радонның маңыздылығын ескере отырып, бұл шолуда радиациядан болатын ықтимал өзгерістерді талқылауға бағытталған.

Түйін сөздер: радиация, радон, эпигенетика, микроРНҚ.

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Эпигенетические модификации и трансгенерационные эффекты, вызванные ионизирующим излучением

Аннотация. В настоящее время ряд стран исследуют различия в экспрессии генов, возникающие в результате изменений метилирования ДНК и модификации структуры хроматина в ответ на внешние раздражители, такие как радиация. Также хорошо известно, что ионизирующее излучение влияет на различные процессы в облученных клетках, в частности, вызывает изменения экспрессии генов, метаболической активности митохондрий, хромосомную нестабильность, апоптоз и другие изменения на молекулярном уровне. Точка зрения о трансгенерационном характере геномной нестабильности предполагает возможное участие эпигенетических механизмов. Казахстан может подвергаться воздействию различных опасных материалов, в том числе радона, радиоактивного газа, который естественным образом образуется в результате непрямого распада урана. Также важно указать, что Республика Казахстан считается лидером по большим запасам урановых руд. Радиоактивное загрязнение считается важным моментом, влияющим как на окружающую среду, так и на здоровье человека. По данным Всемирной организации здравоохранения, хроническое воздействие радона и продуктов его распада является причиной номер один рака легких у некурящих. Все вышеперечисленные факты доказывают, что длительное радиационное загрязнение атмосферы имеет последствия для здоровья нации. Принимая во внимание важность радона как фактора риска рака легких, в этом обзоре основное внимание авторы уделяют обсуждению возможных радиационно-индуцированных изменений.

Ключевые слова: радиация, радон, эпигенетика, микроРНК.

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