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RESEARCH ARTICLE

The activity of metabolic enzymes in the saliva of lung cancer patients

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ABSTRACT

Background: So far, optimization problems for diagnostics and prognostication aids have been still relevant for lung cancer as a leader in the structure of cancers. **Aims and Objectives:** A search for regularities of changes in the saliva enzyme activity in patients with lung cancer. **Materials and Methods:** In the case-control study, 859 people divided into two groups took part: Primary (lung cancer, $n = 286$) and control (conventionally healthy, $n = 573$). All the participants went through a questionnaire survey, saliva biochemical counts, and a histological verification of their diagnosis. The enzyme activity was measured by spectrophotometry. Between group differences were measured with the nonparametric test. **Results:** In terms of lung cancer, we observe metabolic changes described with decreased de Ritis coefficient ($P < 0.001$), as well as the increased activity of alanine aminotransferase ($P = 0.022$), alkaline phosphatase ($P < 0.001$), gamma-glutamyl transpeptidase ($P = 0.043$), and α-amylase ($P < 0.001$). We have identified specifics of the change in the enzyme activity depending on a histological type and a growth form of the tumor. There is the observable increased activity of α-amylase in the saliva in lung adenocarcinoma and neuroendocrine tumors ($P < 0.001$). It has been found that irrespective of the histological type of lung cancer in a transition from central to peripheral forms of growth; there is the observable increased activity of all the enzymes. The significantly reduced activity of aspartate aminotransferase (by 51.4% for adenocarcinoma, $P = 0.032$; 48.8% for squamous cell lung cancer, $P = 0.042$) is a distinctive feature of central lung cancer. **Conclusion:** The nature of the change in the enzyme activity is ambiguous and to a greater degree depends on the tumor form of growth (central/peripheral lung cancer) than the histological type (adenocarcinoma/squamous cell lung cancer).

KEY WORDS: Saliva; Aminotransferase; Lactate Dehydrogenase; Gamma-glutamyl Transpeptidase; Alkaline Phosphatase; α-Amylase

INTRODUCTION

Today, lung cancer is a leader in the structure of cancers.[1-3] At the same time, there is a trend toward an increase in lung cancer morbidity and rejuvenation.[4] In this regard, optimization problems of its diagnostics aids and techniques to prognosticate its run have been still relevant.[5,6]

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Research on specifics of metabolic processes in case of lung cancer, in particular, an activity of some enzymes, is a promising direction.[7] We can consider alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT), alanine transaminase, aspartate aminotransferase (ALT, AST), and α-amylase implicitly informative metabolic enzymes.

It is known that lung cancer cells can produce various enzymes, e.g., α-amylase.[8,9] The increased α-amylase activity

in the blood plasma in lung cancer has been confirmed by a number of papers including those that show that the amylase-producing ability depends on the tumor's histological type.[10] The activity of nicotinamide adenine dinucleotide phosphate (NAD[P])-dependent dehydrogenases, including LDH, causes adjustments in cellular metabolism.[11] Studies have shown that the LDH activity in the blood plasma might be useful as a prognostic factor for both small-cell[12] and non-small cell lung cancer.[13,14] Cancer patients show depressed adaptogenic functions in the body, including those of antioxidant protection.[15] We know about an important role of glutathione in antioxidant lung protection.[16] Some papers have shown that GGT-dependent prooxidant reactions are involved in inhibition of cancer cells proliferation.[17] We have recorded an increased level of GGT in breast cancer,[18] prostate cancer,[19] etc. Monitoring of the ALP activity is widely used to identify cancer metastasis to bone and liver.[20] There are data that support the use of ALP as an informative diagnostic parameter in lung pathologies, including chronic obstructive pulmonary disease, tuberculosis, bronchial asthma, and lung cancer of various histological types.[21] Data on the ALT activity in cancer are scarce and contradictory.[22]

The enzyme activity is conventionally measured in the blood serum and plasma but it is promising to use the saliva as a substrate.[23] The saliva advantages compared with the venous or capillary blood are due to non-invasive sampling and no contamination in time of biomaterial sampling.[24-26] At the same time, the saliva does not only accurately say about a biochemical status and a physiological state of an individual but it is also an implicitly more informative medium to be used in both clinical pathology tests and for separate research purposes.[27-29]

The available sources have not described the saliva used as a material to explore the enzyme activity in lung cancer. Furthermore, note that there are almost no collated data about the activity of all the above-mentioned enzymes including in the blood plasma in patients with lung cancer depending on the histological type and the form of the tumor's growth.

Study Purpose

Find regularities of changes in the enzyme activity in the saliva of patients with lung cancer.

MATERIALS AND METHODS

Study Design

Volunteers divided into 2 groups took part in the case–control study. The first one was primary (with diagnosed lung cancer) and the second one was control (relatively healthy). Grouping was in parallel. Grouping criteria were as follows: Patients aged 30-75, no treatment by time of the study, including surgery, chemotherapy or radiation, no signs of an active infection (including purulent processes), completed oral cavity sanation. Exclusion criteria: Histologically unverified diagnosis.

Patient Recruitment and Sampling

Patients in the main group were examined at the Clinical Oncologic Dispensary (Omsk, The Russian Federation). Patients in the control group were recruited as part of a routine clinical examination at City Polyclinic No. 4 (Omsk, the Russian Federation). Biochemical examinations were performed at the laboratory of KhimServis, LLC (Omsk, the Russian Federation).

Before treatment, all the participants went through saliva sampling in amounts of 2 ml. Saliva samples were given in the morning in fasting state by spitting in sterile test-tubes, then they were centrifuged at 7,000 rpm. Patients in the control group had fluorography testing. Patients in the main group were hospitalized for a radical surgery in the volume of lobectomy bilobectomy, pneumonectomy, combined treatment or video-assisted thoracoscopic surgery for tumor's biopsy. In each case, they went through the histological verification of their diagnosis.

The primary group included patients with the histologically verified lung cancer. The primary group was further divided into subgroups by the following criteria: Histological type of tumor (adenocarcinoma, squamous, and neuroendocrine lung cancer), growth form (central, peripheral cancer, and mediastinal). The control group included relatively healthy patients, who during a routine clinical examination had demonstrated no lung pathology. The saliva of patients in the control group was measured in terms of its biochemical parameters without further division into subgroups.

Aids to Determine Enzyme Activity

The saliva was used as a material for biochemical examinations. The activities of ALT and AST were measured with the colorimetric dinitrophenylhydrazine method of Reitman and Frankel, the Bessey-Lowry-Brock endpoint method to determine ALP, LDH UV-kinetic method by oxidation rate of NADP, GGT-kinetic method using L-gamma-glutamyl-3-carboxy-4-nitroanilide as a substrate for szasz-pierce method, α-amylase kinetic method for 2-chloro-4-nitrophenol (CNP)-oligosaccharide hydrolysis with formation of CNP.[30,31] In addition, the value of de Ritis coefficient was counted as a ratio of the AST/ALT (RU) activity.

Ethical Review

The research was approved at the Ethics Committee Meeting of BIHC for the Omsk Region: "Clinical Oncologic Dispensary" on July 21, 2016, Minutes No. 15.

Statistical Analysis

The statistical analysis was performed using statistica 10.0 software (StatSoft, the USA) and R-package (version 3.2.3) with the nonparametric method using the Mann-Whitney U-test in independent groups and the Wilcoxon's test in dependent groups. Samples were described by calculating the median (Me) and the interquartile amplitude presented as percentiles (25^{th} and 75^{th}) (LQ; UQ). Differences were considered statistically significant at $P < 0.05$.

RESULTS

The study included 286 patients from the Clinical Oncologic Dispensary in Omsk (214 men and 72 women) and 573 apparently healthy individuals selected as a control group. The average age of patients was 58.9 ± 1.1 in the primary group (57.2 ± 2.5 and 60.7 ± 1.1 for women and men, respectively) and 51.9 ± 1.5 in the control group (51.6 ± 1.5 and 52.3 ± 1.7 for women and men, respectively). The primary group included 286 patients with lung cancer of various histological types (squamous cell carcinoma - 88, adenocarcinoma - 143, neuroendocrine tumors - 49 people), and the growth form (central - 87, peripheral - 190, mediastinal form - 9 people).

The findings for the measured activity of salivary enzymes in the examined groups are given in Table 1.

It has been shown that the enzyme activity in the setting of lung cancer is statistically significantly different compared with the control group. Thus, the ALT activity increases by 7.2%. At the same time, the value of de Ritis coefficient reduces by 12.5%. The activity of ALP increases by 30.8%, GGT by 4.8%, and amylase by 57.0% is observably present.

Table 1: The enzyme activity of the saliva as reference and associated with lung cancer

Indicator (u/l)	Control (*n*=573)	Lung cancer (*n*=286)
ALT	3.62 (2.54; 4.85)	3.88 (2.62; 5.54)
	-	*P*=0.022
AST	5.50 (3.75; 7.42)	5.25 (3.00; 7.75)
AST/ALT	1.44 (1.16; 1.96)	1.26 (0.97; 1.70)
	-	*P*<0.001
ALP	56.50 (39.11; 78.23)	73.88 (47.81; 117.34)
	-	*P*<0.001
LDH	1175.0 (692.4; 1850.0)	1148.0 (549.7; 1681.0)
GGT	20.0 (17.3; 23.7)	21.0 (17.8; 24.7)
	-	*P*=0.043
α-amylase	201.6 (100.5; 404.4)	316.5 (160.8; 655.7)
	-	*P*<0.001

P - Statistically significant differences compared with the control group values. ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, LDH: Lactate dehydrogenase, GGT: Gamma-glutamyl transpeptidase

The decrease in the activity was only observed for AST by 4.5% and LDH by 2.3% but it is not statistically significant.

Changes to the enzyme activity essentially depend on the histological type of the tumor (Table 2). Thus, compared with the control group, as for non-small cell lung cancer, there is a statistically significant reduction of the de Ritis coefficient, the LDH activity, as well as the increased activity of ALP, GGT, and α-amylase. For the group of neuroendocrine tumors, there is only an observable increase in the enzyme activity for ALP, LDH, GGT, and α-amylase (46.1, 12.9, 3.5, and 97.6%, respectively). Within the group of non-small cell lung cancer, a change of the enzyme activity is multidirectional. For squamous cell lung carcinoma, there is the maximum reduction of the de Ritis coefficient (−17.4%) and the LDH activity (−17.5%); among the examined groups, we have observed the lowest activity for ALP (+25.0%), GGT (+4.0%), and α-amylase (+15.4%). For adenocarcinoma, increases in activity of ALP (+46.1%), α-amylase (+76.0%), and GGT (+8.0%) are maximum, while the LDH activity does not differ from the normal range.

We further evaluated the saliva enzyme activity among lung cancer patients depending on the form of the tumor growth (Table 3). It is shown that compared with the control group, in all the examined groups, the ALT activity is increased, at the same time, the maximum value has been found for peripheral lung cancer (+12.7%). The AST activity is only reduced in case of central lung cancer, whereas the value of the de Ritis coefficient declines for all the groups, while the maximum reduction is observed for central lung cancer. The ALP activity increases from the mediastinal form of lung cancer to central and then peripheral (11.5; 23.1, and 46.1%, respectively). There is the same direction for the increase in the LDH activity (−43.9, −15.3, and +2.7%, respectively). Dynamics of the change of GGT and α-amylase activities is of the same type. For central lung cancer, the GGT activity corresponds to the reference value but against the background of peripheral and mediastinal forms of growth, the GGT activity is higher (7.0% and 16.0%, respectively). The α-amylase activity is the minimum for central lung cancer (+26.0%), increasing in the transition to peripheral lung cancer (57.4%), and then the mediastinal form (+73.4% compared with the control group).

Note that statistically significant differences have been only found between central and peripheral lung cancers for the AST activity *(P* = 0.009), de Ritis coefficient (*P* = 0.037), and the LDH activity (*P* = 0.044). For all the other groups, the differences are only statistically significant in comparison with the control group (Tables 2 and 3).

To determine what contributes most to differences between the examined groups (tumor's histological type or form of growth), we compared the activity of enzymes in case of adenocarcinoma and squamous cell lung cancer, depending

Table 2: The enzyme activity of the saliva in healthy people and in people associated with lung cancer, depending on the tumor's histological type

Indicator (u/l)	NSCLC (*n*=237)	PLC (*n*=88)	AC (*n*=143)	NEC (*n*=49)
ALT	3.77 (2.62; 5.40)	3.77 (2.58; 5.23)	3.77 (2.62; 5.77)	4.31 (2.54; 6.54)
	-	-	-	*P*=0.030
AST	5.17 (2.92; 7.50)	4.74 (3.00; 6.96)	5.25 (2.75; 7.75)	5.75 (3.67; 9.33)
	-	*P*=0.047	-	-
AST/ALT	1.25 (0.94; 1.66)	1.19 (0.95; 1.61)	1.27 (0.93; 1.70)	1.34 (1.07; 1.77)
	P<0.001	*P*<0.001	*P*<0.001	-
ALP	71.71 (45.63; 115.17)	70.62 (49.98; 99.96)	82.57 (45.63; 126.03)	82.57 (54.33; 117.34)
	P<0.001	*P*<0.001	*P*<0.001	*P*<0.001
LDH	1108.0 (549.7; 1665.0)	969.2 (446.9; 1653.0)	1159.0 (576.6; 1674.0)	1326.0 (613.4; 1850.0)
	P=0.037	*P*=0.034	-	-
GGT	21.3 (17.7; 24.7)	20.8 (17.7; 24.7)	21.6 (17.9; 25.0)	20.7 (18.8; 24.9)
	P=0.049	-	*P*=0.045	-
α-amylase	301.6 (139.7; 662.4)	232.6 (99.5; 357.9)	354.8 (213.3; 741.5)	398.3 (207.3; 617.1)
	P=0.002	-	*P*<0.001	*P*=0.007

P - Statistically significant differences compared with the control values, NSCLC: Non-small cell lung cancer, ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, LDH: Lactate dehydrogenase, GGT: Gamma-glutamyl transpeptidase, PLC: Pleural lavage cytology

Table 3: The enzyme activity of the saliva in healthy people and people associated with lung cancer, depending on the tumor's growth shape

Indicator (u/l)	Central lung cancer (*n*=87)	Peripheral lung cancer (*n*=190)	Mediastinal form of LC (*n*=9)
ALT	3.77 (2.54; 5.08)	4.08 (2.69; 5.85)	3.85 (2.31; 6.46)
	-	P_1=0.004	-
AST	4.42 (2.58; 6.33)	5.50 (3.42; 8.17)	5.50 (3.67; 8.08)
	P_1=0.003	P_2=0.009	-
AST/ALT	1.17 (0.83; 1.58)	1.31 (1.01; 1.73)	1.18 (1.02; 1.59)
	P_1<0.001	P_1=0.002, P2=0.037	-
ALP	69.54 (47.81; 95.61)	82.57 (45.63; 126.03)	63.02 (54.33; 86.92)
	P_1=0.003	P_1<0.001	-
LDH	995.5 (482.6; 1550.0)	1206.3 (559.5; 1855.0)	659.2 (370.9; 1233.0)
	P_1=0.019	P_2=0.044	-
GGT	20.3 (17.5; 23.6)	21.4 (18.1; 25.2)	23.2 (20.4; 28.0)
	-	P_1=0.018	P_1=0.047
α-amylase	254.0 (145.3; 796.8)	317.4 (160.8; 599.0)	349.6 (250.4; 1107.0)
	P_1=0.046	P_1<0.001	-

P_1 - Statistically significant differences compared with the control values, P_2 - Statistically significant differences compared with the values for central lung cancer. ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, LDH: Lactate dehydrogenase, GGT: Gamma-glutamyl transpeptidase

on the growth form (Table 4). We have found that irrespective of the histological type of lung cancer, in the transition from the central to the peripheral form of growth, there is the observed increase in activity of all the enzymes. The difference in the activity of ALT is statistically significant; the ALT activity is increasing by 28.3% and 10.6%, whereas the increase in the AST activity was 51.4% and 48.8% for adenocarcinoma and squamous cell carcinoma, respectively. The value of the de Ritis coefficient is increasing in the same direction. However, the comparison with the control group (Table 1) has shown that for peripheral lung cancer the AST activity corresponds to reference values, whereas for the central form of growth, the AST activity is significantly lower. For the remaining enzymes, the activity against the background of central lung cancer is closer to values corresponding to the control group; for the peripheral form of growth, deviations are highest. The α-amylase is the only enzyme the activity of which to a greater degree depends on the histological type of the tumor, differences in its activity for adenocarcinoma and squamous cell lung cancer are statistically significant (P_2 = 0.017).

Table 4: Comparison of enzyme activity in adenocarcinoma and squamous cell lung cancer depending on a growth form

Indicator (u/l)	Adenocarcinoma		Squamous lung cancer	
	Central (*n*=28)	Peripheral (*n*=115)	Central (*n*=40)	Peripheral (*n*=48)
ALT	3.15 (2.23; 4.31)	4.04 (2.69; 5.92)	3.69 (2.62; 4.73)	4.08 (2.31; 5.23)
	-	*P*1=0.047	-	-
AST	3.58 (1.83; 6.92)	5.42 (3.33; 7.79)	3.75 (2.83; 5.54)	5.58 (3.17; 8.00)
	-	P_1=0.032	-	P_1=0.042
AST/ALT	1.19 (0.73; 1.69)	1.29 (1.00; 1.71)	1.16 (0.75; 1.57	1.25 (1.03; 1.81)
ALP	70.62 (46.72; 101.04)	82.57 (41.29; 130.38)	69.54 (52.15; 85.83)	73.88 (49.98; 108.65)
LDH	1127.0 (546.3; 1647.0)	1160.0 (580.1; 1711.0)	945.0 (534.9; 1456.5)	1193.0 (437.7; 1846.0)
GGT	19.6 (15.7; 23.7)	21.9 (18.5; 25.2)	20.0 (17.7; 22.8)	21.4 (17.6; 25.8)
α-amylase	274.2 (165.4; 650.0)	399.3 (263.6; 747.9)	232.6 (73.3; 839.2)	250.1 (119.2; 312.0)
	-	P_2=0.017	-	-

P_1 - Statistically significant differences compared with values for central lung cancer of a corresponding histological type, P_2 - Statistically significant differences between corresponding forms of lung cancer growth. ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, LDH: Lactate dehydrogenase, GGT: Gamma-glutamyl transpeptidase

DISCUSSION

The regularities for changes in the saliva enzyme activity of patients with lung cancer have been identified. It has been shown that the tumor's form of growth has more influence on the saliva enzyme activity than the histological type of lung cancer. The parameters have been identified that make it possible to draw a mutual distinction between patients from the control group and primary group and patients with squamous cell lung carcinoma and adenocarcinoma.

In terms of lung cancer, there are observable metabolic changes, described with the lower de Ritis coefficient at the expanse of the increased ALT activity accompanied with the increased activity of GGT and ALP, as well as dropped LDH activity (Table 1). GGT is an enzyme responsible for transportation of amino acids into cells; the increased GGT activity enhances an input of amino acids through a cell membrane. The dropped LDH activity means total inhibition in energy systems. It is known that in the blood of lung cancer patients; there is the reduced activity of NAD- and NADP-dependent dehydrogenases, including LDH, which means less intensive aerobic and anaerobic energy processes.[7] The increased ALT activity might be also seen as a strengthened contribution of glucose-alanine pathway with a release of glucose from cell due to its dephosphorylation in terms of the high ALP activity. ALP is involved in processes of transmembrane phosphorylation and together with the hormone system ensures a glucose input and output from cells, directly affecting blood glucose levels and contributing into maintaining the phosphate content required for bioenergy. In this regard, there are observable inhibited final pathways of glucose metabolism, as evidenced by the low AST activity, involved in making the de Ritis coefficient lower. Such changes in the enzyme activity might reflect stimulation of peripheral exchange zones, particularly protein, against inhibited central metabolic pathways.

Specifics of changes in the saliva enzyme activity depending on the histological type of the tumor (Table 2) has been identified. It is known that the most pronounced increase in the activity of a number of metabolic enzymes in cells of both healthy and tumorous lung tissues is detected in patients with adenocarcinoma.[32] In particular, increased expression of α-amylase is typical for lung adenocarcinoma, consistent with our findings.[8] It is also known that the α-amylase level in the pleural fluid correlates with lung cancer development, especially adenocarcinoma.[33] However, in neuroendocrine tumors, the salivary α-amylase activity is 12.3% higher than in terms of adenocarcinomas that had not been previously described in the literature. The increased activity of the salivary α-amylase might be a response to the development of systemic endogenous toxicity,[34] more pronounced in case of neuroendocrine tumors, particularly, small cell lung cancer.[35]

GGT is also one among detoxifying systems in the body. It is involved in destruction of serotonin, histamine, and proteolysis of denatured proteins. GGT might be considered a marker of intoxication.[36] A statistically significant increase in the GGT activity has been only found in small cell lung cancer, in particular, adenocarcinoma (Table 2).

The ALP activity is 46.1% higher in terms of adenocarcinomas and neuroendocrine tumors than in the control group, which correlates with literature data.[21] It is known that for adenocarcinoma a higher level of oxidative phosphorylation is typical, for squamous cell lungs carcinoma - A higher rate of glycolysis,[37] which might be a factor for a disproportionate increase in the ALP activity in lung adenocarcinoma. Overall, in terms of lung cancer, the ALP activity is increased validating feasibility for a wider application of this parameter.[38]

The review of the LDH activity has shown that neuroendocrine tumors are described with the increased activity of this

enzyme, while squamous cell lung cancer with the decreased one (Table 2). In a number of papers, it is shown that the high level of LDH in small-cell lung cancer is an unfavorable prognostic sign associated with a low response to an administered therapy,[39] similar results have been obtained for adenocarcinoma.[40] Being an enzyme involved in anaerobic metabolism, LDH can influence a malignant potential of the tumor through various mechanisms, including increased proliferation, survival rate and invasive capacity of tumor cells, as well as reduced apoptosis.[41,42]

Note that only in squamous cell lung carcinoma, there was a statistically significant decrease in the AST activity by 13.8% compared to the control group, preconditioning the most significant decrease in the de Ritis coefficient. The described changes say about more severe hypoxia features in squamous cell lung carcinoma.[43,44]

The identified changes in the activity of metabolic enzymes in lung cancer of various histological types show that hypoxia is a factor that conditions the metabolic shift. However, hypoxic features should be implicitly unevenly manifested for peripheral and central lung cancers. There are known clinical differences between central and peripheral squamous lung cancers.[45] According to completed tests, for central lung cancer the lower activity of metabolic enzymes is typical (Table 3). Dynamics of the enzyme activity repeats the previously described one for squamous cell lung cancer (Table 2). It is of interest that in mediastinal lung cancer we also observe the reduction of the de Ritis coefficient at the expense of the increased activity of ALT, whereas the AST activity corresponds to its reference value. The distinct increase in the activities of GGT and α-amylase is probably a response to evolving endogenous intoxication. However, the ALP activity is slightly increasing, while for LDH a decrease by 43.9% is typical compared with the reference value, which might be explained with an absence of a primary tumor lesion.

By further subgrouping of lung cancer patients with various histological types by the form of their tumor growth, we have shown that adenocarcinoma and squamous cell lung cancer show changes of the same type in the enzyme activity in the transition from central to peripheral lung cancer (Table 4). The main difference between the examined histological types of the lung is the α-amylase activity as it is α-amylase that is produced by lung adenocarcinoma cells as confirmed by numerous research.[8-10,32-34] Other than that, a hallmark for central lung cancer is the significantly reduced AST activity, reducing the value of the de Ritis coefficient that might point out to decreased intensity in oxidative phosphorylation. The enzyme activity is increasing in the transition from central to peripheral lung cancer. In case of GGT and α-amylase, this results in more expressed features of endotoxemia. The higher activity of ALT and ALP might result in increased glycolysis and increasing hypoxic features. It is known that in the tumor tissues, there are ongoing changes in oxygen pressure, lung tumors, average oxygen pressure is 2.2 mm Hg, pointing out to hypoxia.[46] The low oxygen content causes gene expression toward a more aggressive phenotype, hypoxia also reduces sensitivity to therapy.[47,48] All the above-mentioned should be considered to develop treatment strategies and to estimate the efficacy of an administered therapy.

Limiting factors in the completed research are associated with a small number of enzymes covered by the research. In particular, among the promising directions, there is the activity evaluation for the antioxidant enzymes, ALP, and LDH isoenzymes to make more precise and to expand revealed regularities. Grounding an application of findings is also promising for monitoring of the disease, which requires research of dynamics in examined parameters on the background of different treatment types, including chemotherapy and radiation.

CONCLUSIONS

In the setting of lung cancer, the change of the activity of metabolic enzymes is observed. The nature of the change in the enzyme activity is ambiguous and more dependent on a form of the tumor growth (central/peripheral lung cancer) than the histological type (adenocarcinoma/squamous cell lung cancer). Therefore, estimating the enzyme activity, it is not only necessary to match obtained values with reference counts but also to consider a tumor's growth form and its histological type. Overall, the findings might be used to enhance the efficiency of traditional aids for diagnostics, prognostication of the disease run, treatment monitoring, etc.

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