**INTRODUCTION**

Lung cancer, predominantly nonsmall cell lung cancer (NSCLC), is the leading cause of cancer-related death worldwide. \(^1,2\) It has been documented that, especially in well-developed countries, the incidence and mortality due to lung cancer remain at a very high and constant level, particularly among men. \(^3,4\) However, recently, the more frequent incidence among women has been observed. \(^5\)

According to histopathological verification, lung cancer is classified into 2 major groups based on its biological phenotype, therapy, and prognosis: nonsmall cell lung cancer (NSCLC), including squamous cell carcinoma (SCC) and nonsquamous cell carcinoma (NSCC), which accounts for approximately 85% of all primary lung cancers and small cell lung cancer (SCLC), which constitutes about 15% of malignant cases. SCLC is widely recognized as a disease strongly associated with tobacco addiction. \(^6\)

The prognosis in lung cancer is poor (5-year overall survival rate does not exceed 15%), and, moreover, the difficulties in diagnosis at an early stage of the disease are well-documented (up to

**OBJECTIVES**

In the present study, we evaluated the association of SNPs (rs744 166 [AG] and rs3 816 769 [CT]) with predisposition to nonsmall cell lung cancer (NSCLC) development and their potential effect on STAT3 expression.

**RESULTS**

STAT3 CC (rs3 816 769) and AA genotypes (rs744 166) were associated with lower lung cancer risk, whereas TT (rs3 816 769) and GG genotypes (rs744 166) were found to be associated with significantly elevated lung cancer risk. In the NSCLC group, odds ratio analysis showed that allele A was rare and might be linked with decreased while allele G with increased lung cancer risk. We demonstrated that overexpression of STAT3 positively correlated with TT genotype (rs3 816 769) in NSCLC patients \((P = 0.0464)\). Moreover, the differences in STAT3 gene expression between squamous cell carcinoma and large cell carcinoma histopathological subtypes were observed.

**CONCLUSIONS**

It has been shown that rs3816769 STAT3 gene polymorphisms are associated with NSCLC susceptibility and might be regarded as having a significant functional and diagnostic value.

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**KEY WORDS**

nonsmall cell lung carcinoma, STAT3, gene expression, single nucleotide polymorphisms

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**ABSTRACT**

Lung cancer, predominantly nonsmall cell lung cancer (NSCLC), is the leading cause of cancer-related death worldwide. \(^1,2\) It has been documented that, especially in well-developed countries, the incidence and mortality due to lung cancer remain at a very high and constant level, particularly among men. \(^3,4\) However, recently, the more frequent incidence among women has been observed. \(^5\)

According to histopathological verification, lung cancer is classified into 2 major groups based on its biological phenotype, therapy, and prognosis: nonsmall cell lung cancer (NSCLC), including squamous cell carcinoma (SSC) and nonsquamous cell carcinoma (NSCC), which accounts for approximately 85% of all primary lung cancers and small cell lung cancer (SCLC), which constitutes about 15% of malignant cases. SCLC is widely recognized as a disease strongly associated with tobacco addiction. \(^6\)

The prognosis in lung cancer is poor (5-year overall survival rate does not exceed 15%), and, moreover, the difficulties in diagnosis at an early stage of the disease are well-documented (up to
40% of the cases are diagnosed at the advanced stage IIB-IIIA. Therefore, advances in identification of genetic factors that affect susceptibility to lung cancer, especially NSCLC, could be of great value.

Among many recognized genetic factors relevant for NSCLC, including mutations, polymorphisms, and overexpression of more than 30 genes, such as: K-Ras, BRAF, TP53, MYC, cyclin D1, EGFR, C-erbB2 (Her-2/neu) or BCL2, the significance of STAT3 molecular lesions have not been fully elucidated. As an important member of the STAT protein family, STAT3 participates in tumor cell survival, proliferation, migration, invasion, angiogenesis, and inhibition of apoptosis in many types of human cancer, including lung cancer. Moreover, the association between single nucleotide polymorphisms (SNPs) of STAT3 and susceptibility to carcinogenesis has been confirmed. Additionally, it has been recognized that increased expression of STAT3 correlates with tumor progression and invasiveness; however, the causal mechanism of this molecular alteration and its prognostic value still remain unclear. Up to now, there have been few studies focused on SNPs in the STAT3 gene and their effect on gene expression, as well as their correlation with NSCLC risk, especially in the European population. The recently published study has documented the correlation of STAT3 expression with growth, survival, and radio resistance of NSCLC cells. The significance of some STAT3 SNPs in NSCLC and also in acute myeloid leukemia (AML) has been reported in the Asian population, but there was no correlation with gene expression.

Therefore, in the present study we decided to examine whether the selected STAT3 SNPs affect the NSCLC risk and/or expression of STAT3. We also evaluated their diagnostic value in NSCLC patients.

**PATIENTS AND METHODS**

**Subjects** The study was approved by the Ethical Committee of the Medical University of Lodz, Poland. We enrolled 71 patients with diagnosed NSCLC who had undergone lobectomy at the Department of Chest Surgery, General and Oncological Surgery University Hospital No. 2, Medical University of Lodz. Tumor tissue fragments (100–150 mg) from each patient were obtained from the center of lung lesion and the macroscopically unchanged lung tissue served as a calibrator sample. Lung tissue samples were collected into lysis buffer (Buffer RNA later) and frozen at ~70°C until use, immediately after collection. Additionally, blood samples (5 ml) were obtained from each NSCLC patient and control subject for an SNP analysis. The control group consisted of 104 persons without NSCLC diagnosis, other tumors, or chronic disease. They were collected during the routine laboratory analysis. Clinical characteristics of the patients and control group are presented in **Table 1**.

Macroscopically unchanged lung tissue served as a reference standard (calibrator) in expression analysis. The smoking history of all studied patients (64 with diagnosed NSCLC and 82 as a control group) are available. Patients were divided into groups according to their smoking habits: the period of tobacco addiction and the amount of cigarettes smoked – the latter was presented as pack years and was calculated according to the NCI Dictionary of Cancer Terms (1 pack year is equal to smoking 20 cigarettes per day for 1 year).

**DNA extraction and SNP genotyping** Two SNPs in the STAT3 gene, rs744166, and rs3816769, have been selected based on the previously published reports regarding their association with lung cancer risk and a significant role in inflammation. Genomic DNA from patients and the control group was isolated from blood samples using Qiagen QIAamp DNA Mini Kit, according to the manufacturer’s procedure. The SNP analysis was performed using TaqMan SNP genotyping assays (Applied Biosystems, USA): C_3140282_10 (rs744166) and C_3140296_10 (rs3816769). SNPs were selected based on the previously published reports and related to STAT3 genotyping.

**RNA extraction, relative expression of STAT3** Total RNA was extracted from tissues, using RNeasy Protect Kit (EURLX, Poland) and according to the manufacturer’s instructions. Complementary DNA (cDNA) was transcribed from 100 ng of total RNA, using a High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems, United States) at a total volume of 20 μl per reaction. Reverse transcription (RT) master mix contained: 10 × RT buffer, 25 × dNTP Mix (100 mM), 10 × RT Random Primers, MultiScribe™ Reverse Transcriptase, RNase Inhibitor, and nuclease-free water. RT reaction was performed in a Personal Thermocycler (Eppendorf, Germany) under the following conditions: 10 minutes at 25°C, followed by 120 minutes at 37°C; then the samples were heated to 85°C for 5 s, and held at 4°C.

The relative expression of STAT3 was assessed using TaqMan probes for STAT3 (Hs01047580_m1) and ACTB (Hs99999903_m1), as the reference gene, in Applied Biosystems 7900HT Fast Real-Time PCR System for 39 cycles. The PCR mixture contained: cDNA (1 to 100 ng), 20 × TaqMan® Gene Expression Assay, 2 × TaqMan® Gene Expression Master Mix, RNase-free water in total volume of 20 μl. Macroscopically unchanged tissue served as a calibrator sample. The relative expression of each sample was assessed using the Comparative CT method (TaqMan Relative Quantification Assay) and presented as the relative quantification (RQ) value. The RQ values for STAT3 were calculated using the delta CT method and adjusted to the β-actin expression and relative to the expression level of calibrator, for which RQ was equal 1.
The frequencies of the studied genotypes (AA, AG, GG) and OR values for \textit{STAT3} rs744166 polymorphism in NSCLC patients compared with controls are shown in Table 2.

The results revealed a significant association of GG genotype and G allele in rs744166 with increased lung cancer risk (OR, 2.60; \( P = 0.04 \); OR, 2.29; \( P = 0.034 \)). We observed a statistically significant (\( P < 0.05 \)) decrease in the frequency of AA genotype (OR, 0.41; \( P = 0.012 \)) and A allele (OR, 0.44; \( P = 0.034 \)) in NSCLC.

The frequencies of the studied genotypes (CC, CT, TT) and OR values for \textit{STAT3} rs3816769 polymorphism in NSCLC patients compared with controls are shown in Table 3.

Furthermore, the results revealed significant association of the CC genotype in rs3816769 with increased lung cancer risk (OR, 0.26; \( P = 0.043 \)). We also observed a statistically significant

\[ \chi^2 \] analysis

\[ \text{Pearson} \] chi-square

\[ \text{postoperatively Tumor Node Metastasis Classification}^{1,2,8} \]

Abbreviations: AC – adenocarcinoma, LCC – large cell carcinoma, NSCLC – nonsquamous cell carcinoma, SCC – squamous cell carcinoma, SD – standard deviation

### RESULTS Genotyping analysis

A statistical analysis of the frequency of the studied alleles and genotypes of \textit{STAT3} confirmed the presence of significant differences between the studied groups (NSCLC vs. control). The frequencies of the studied genotypes (AA, AG, GG) and OR values for \textit{STAT3} rs744166 polymorphism in NSCLC patients compared with controls are shown in Table 2.

The results revealed a significant association of GG genotype and G allele in rs744166 with increased lung cancer risk (OR, 2.60; \( P = 0.04 \); OR, 2.29; \( P = 0.034 \)). We observed a statistically significant (\( P < 0.05 \)) decrease in the frequency of AA genotype (OR, 0.41; \( P = 0.012 \)) and A allele (OR, 0.44; \( P = 0.034 \)) in NSCLC.

The frequencies of the studied genotypes (CC, CT, TT) and OR values for \textit{STAT3} rs3816769 polymorphism in NSCLC patients compared with controls are shown in Table 3.

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Data are presented as mean ± standard deviation or number (percentage).

\[ \chi^2 \] analysis

\[ \text{Pearson} \] chi-square
orIGInAL ArtIcLE

STAT3 rs3816769 polymorphism correlates with gene expression level...

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with regard to histopathological NSCLC subtype, tumor staging, patients’ age, sex, and smoking history, as well as to STAT3 polymorphism. In each histopathological NSCLC subtype, the increased expression (RQ value >1) was observed for more than 70% of the cases. The highest expression level of STAT3 in NSCLC was observed for the SCC subtype (mean RQ, 7.34) and the lowest in LCC (mean RQ, 1.73). The results of the relative quantification analysis in individual histopathological NSCLC subtypes, indicating mean RQ values, as well as the number of samples with increased (RQ >1) and decreased (RQ <1) STAT3 expression are shown in TABLE 4.

A statistical analysis revealed the differences in RQ values between all studied histopathological

relative

STAT3 expression analysis

The RQ values were compared between NSCLC patients with regard to histopathological NSCLC subtype, tumor staging, patients’ age, sex, and smoking history, as well as to STAT3 polymorphism. In each histopathological NSCLC subtype, the increased expression (RQ value >1) was observed for more than 70% of the cases. The highest expression level of STAT3 in NSCLC was observed for the SCC subtype (mean RQ, 7.34) and the lowest in LCC (mean RQ, 1.73). The results of the relative quantification analysis in individual histopathological NSCLC subtypes, indicating mean RQ values, as well as the number of samples with increased (RQ >1) and decreased (RQ <1) STAT3 expression are shown in TABLE 4.

A statistical analysis revealed the differences in RQ values between all studied histopathological

Abbreviations: OR – odds ratio, CI – confidence interval

TABLE 2

Frequencies of STAT3 rs744166 genotypes (A/A, A/G, G/G) as well as A and G alleles and odds ratio in patients with nonsmall cell lung cancer compared with the control group

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients, n = 71</th>
<th>Controls, n = 104</th>
<th>OR (CI 95%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number</td>
<td>frequency</td>
<td>number</td>
<td>frequency</td>
</tr>
<tr>
<td>AA</td>
<td>18</td>
<td>0.25</td>
<td>47</td>
<td>0.45</td>
</tr>
<tr>
<td>AG</td>
<td>21</td>
<td>0.30</td>
<td>32</td>
<td>0.31</td>
</tr>
<tr>
<td>GG</td>
<td>32</td>
<td>0.45</td>
<td>25</td>
<td>0.24</td>
</tr>
<tr>
<td>χ² = 3.49</td>
<td></td>
<td>χ² = 3.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>allele A</td>
<td>57</td>
<td>0.40</td>
<td>126</td>
<td>0.60</td>
</tr>
<tr>
<td>allele G</td>
<td>85</td>
<td>0.60</td>
<td>82</td>
<td>0.40</td>
</tr>
</tbody>
</table>

* χ² test <3.991; P > 0.05

Abbreviations: see TABLE 1

TABLE 3

The frequencies of STAT3 rs3816769 genotypes (C/C, C/T, T/T) as well as C and T alleles and odds ratio in patients with nonsmall cell lung cancer compared with the control group

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients, n = 71</th>
<th>Controls, n = 104</th>
<th>OR (CI 95%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number</td>
<td>frequency</td>
<td>number</td>
<td>frequency</td>
</tr>
<tr>
<td>CC</td>
<td>11</td>
<td>0.15</td>
<td>43</td>
<td>0.41</td>
</tr>
<tr>
<td>CT</td>
<td>24</td>
<td>0.34</td>
<td>35</td>
<td>0.33</td>
</tr>
<tr>
<td>TT</td>
<td>36</td>
<td>0.51</td>
<td>26</td>
<td>0.25</td>
</tr>
<tr>
<td>χ² = 3.70</td>
<td></td>
<td>χ² = 2.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>allele C</td>
<td>46</td>
<td>0.32</td>
<td>121</td>
<td>0.58</td>
</tr>
<tr>
<td>allele T</td>
<td>96</td>
<td>0.68</td>
<td>87</td>
<td>0.42</td>
</tr>
</tbody>
</table>

* χ² test <3.991; P > 0.05

Abbreviations: see TABLE 2

TABLE 4

Expression levels of the STAT3 gene (RQ values) in individual histopathological subtypes of nonsmall cell lung cancer calculated by the delta-delta computed tomography method

<table>
<thead>
<tr>
<th>Histopathological NSCLC subtype</th>
<th>Mean RQ value (range)</th>
<th>Number (percentage) of samples with</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RQ value &gt;1</td>
</tr>
<tr>
<td>SCC (n = 41)</td>
<td>7.34 (0.01–137.98)</td>
<td>29 (71%)</td>
</tr>
<tr>
<td>AC (n = 23)</td>
<td>2.75 (0.38–20.31)</td>
<td>17 (74%)</td>
</tr>
<tr>
<td>LCC (n = 7)</td>
<td>1.73 (0.11–5.90)</td>
<td>5 (72%)</td>
</tr>
<tr>
<td>total (n = 71)</td>
<td>3.94 (0.01–137.98)</td>
<td>51 (72%)</td>
</tr>
</tbody>
</table>

Abbreviations: RQ – relative quantification, others – see TABLE 1

(P < 0.05) decrease in the frequency of TT genotype (OR 3.1, P = 0.02) in NSCLC.

No association was found between the studied polymorphisms and NSCLC histopathological subtype, tumor clinical staging (pTNM classification) as well as patients’ age, sex, and smoking history. A haplotype analysis showed no significant difference between the study and control groups.

The STAT3 rs3816769 polymorphism is in a strong linkage disequilibrium (D’ = 0.923; r² = 0.61) with the neighboring rs744166 polymorphism in the studied Polish population.

Relative STAT3 expression analysis

The RQ values were compared between NSCLC patients...
subtypes ($P = 0.0152$; Kruskal–Wallis test), as presented in Figure 1. A significant difference was observed between squamous cell carcinoma (SCC) and large cell carcinoma (LCC) (Neuman–Keuls multiple comparison test).

There was no significant difference in RQ values and the clinical features of the studied NSCLC patients, i.e., patients’ age, sex, and history of smoking (assessed as pack years) ($P > 0.05$; Kruskal–Wallis, Mann–Whitney’s test, and Spearman’s rank correlation coefficient).

The significant correlation between RQ values and STAT3 rs3 816 769 SNP was observed for TT genotype ($P = 0.046$; Kruskal–Wallis test, Neuman–Keuls multiple comparison test), as presented in Figure 2. The analysis did not reveal any significant association between the expression level of STAT3 and occurrence of rs744 166 SNP ($P = 0.132$; Kruskal–Wallis test).

**Discussion** Numerous data have shown that oncogenic STAT3 and its polymorphic variants are implicated in the development of various types of human cancer, including lung cancer.\(^{22,26,31,32}\) It has been suggested that some inherited STAT3 polymorphisms may correlate with STAT3 expression and may be implicated via constitutive SOCS3 expression in cancer progression as well as survival of cancer cells.\(^{33,34}\) In the present study, we evaluated the association between 2 SNPs (rs744 166 and rs3 816 769) in the STAT3 gene and the risk of NSCLC development in Polish patients and additionally assessed the effect of the studied SNPs on STAT3 expression. According to our knowledge, it is the first study focused on European NSCLC patients.

Our study confirmed significant roles of both studied SNPs (rs744 166 and rs3 816 769) in the susceptibility to lung cancer development. The obtained results indicate that the presence of TT genotype (rs3 816 769) and GG genotype (rs744 166) might increase the risk of NSCLC development, while CC genotype (rs3 816 769) and AA genotype (rs744 166) might decrease the risk of lung cancer. In the Chinese population study, where several SNPs (e.g., rs4796793, rs7211777, rs12949 918, rs4796793, rs7211777, rs12949 918, rs9912773, and rs3869550) were investigated, the association between SNP rs744 166 and the risk of NSCLC development was also shown,\(^{35}\) which is in line with our data. However, contrary to our results, the study performed by Jiang et al.\(^{36}\) showed that carriers of the minor G allele (rs744 166) and GG genotype had a decreased risk of NSCLC, while the presence of A allele and AA genotype seemed to have a protective effect. Similarly, based on the study regarding Crohn’s disease, a significantly decreased risk of this syndrome was observed in individuals carrying G allele in SNP rs744 166 of STAT3.\(^{30}\)

The opposite results regarding the frequency of polymorphic variants of the STAT3 gene (rs744 166) and their association with the disease may suggest the population discrepancies. Additionally, these differences may suggest different types of inflammatory mechanisms, which are implicated in the induction of various types of tumors and diseases with chronic, nonspecific inflammation.\(^{37}\) It is known that the enhanced production of pleiotropic interleukin 6 and tumor necrosis factor leads to inflammation and activation of the oncogenic transcription factor STAT3,\(^{36,37}\) which plays a role in the immune system regulation. Moreover, the STAT3/IL-6 signaling pathway as a major mediator of the inflammatory response and host defense is involved in tumor cell survival owing to the progression of the neoplastic growth. Activated via phosphorylation, STAT3 upregulates tumor angiogenesis, metastasis, and invasion and inhibits tumor cell apoptosis.\(^{37}\) In the light of this observation, STAT3 polymorphic variants and their expression associated with high IL-6 levels seem to be important in chronic inflammatory disease as well as in inflammatory-related cancer, including lung cancer.
It should be stressed that the study by Ferguson et al., focused on Crohn's disease confirmed the significance of the STAT3 gene SNPs in its etiopathology. It also provides indirect evidence that STAT3 gene variants may be important in the development of inflammatory-related cancer (e.g., colorectal malignances). In particular, a significantly decreased risk of Crohn's disease was observed in individuals carrying the C allele and the genotype CC in rs3816769 SNP of the STAT3 gene. Considering this result, in our study, we decided to investigate if there is any correlation between rs3816769 SNP and lung cancer. Our results concerning this polymorphism are similar to those obtained by Ferguson et al. in Crohn's disease. Unfortunately, we are unable to compare our results with respect to lung cancer or other types of human cancers, because there are no publications available focused on this issue.

We also evaluated the association between the studied SNPs and histopathological features of tumors (pTNM staging) and clinical characteristics of the patients and found no correlations. It is in contrast to the study performed by Jiang et al. in the Chinese population, who found that AG or GG genotypes (rs744166) may have a protective value, especially in stage III/IV of lung cancer.

In our study, we focused also on the correlation of STAT3 SNPs with gene expression. Results of our analysis suggest an association of rs3816769 with STAT3 expression. It should be stressed that our observation did not unambiguously confirm the functional significance of the studied SNP. We did not recognize the presence of the differences in STAT3 expression levels in correlation with the studied SNP separately for normal tissue. However, our findings are of value given the lack of similar studies concerning assessment of STAT3 variants and their correlation with the gene expression level and NSCLC risk.

We also observed high linkage disequilibrium between the two studied SNPs in Polish NSCLC patients. The expression analysis assessing STAT3 mRNA level in lung cancer patients revealed an increased gene expression in the majority of the studied NSCLC samples. To the best of our knowledge, the overexpression of STAT3 at mRNA level has been observed in 2 types of human cancers, such as colorectal cancer and cervical squamous cell carcinoma. The only study focused on STAT3 expression in lung cancer regarded SCLC and concerning protein level has been published. The results obtained in the above study showed positive correlations of STAT3 protein expression with lymph node metastasis, clinical stage, and tumor size.

Additionally, the association between the overexpression of STAT3, pSTAT3, and some tumor parameters, such as the size and necrosis in different human soft tissue cancers was observed. In our present study, a significantly increased STAT3 expression was revealed in SCC, which is the most frequent and heterogeneous subtype of NSCLC. Regarding patient characteristics, we did not find any association with the STAT3 expression level. Because there have been no similar studies, concerning NSCLC, we cannot compare our results with those of other investigators. However, STAT3 overexpression and its positive association with SCC observed in our study might have an important diagnostic value, aiming at an accurate subclassification between SCC and adenocarcinoma, especially in the context of the latest research on new diagnostic algorithms based on molecular lesions and improving personalized treatment of NSCLC.

Concluding, the presented results confirmed the association between the chosen STAT3 polymorphisms and susceptibility to NSCLC development. It should be emphasized that the most important result of our analysis was the correlation found between the increased gene expression level and TT genotype (rs3816769), which additionally revealed the association with NSCLC risk in our study group. On the other hand, CC genotype (rs3816769) (association with decreased gene expression) might decrease lung cancer risk. The association between an increased STAT3 expression and SCC histopathological subtype might draw attention to this gene as a potential diagnostic marker. It is worth noting that our study focus on the Polish population and may confirm universally accepted hypothesis concerning a significant role of STAT3 gene as well as JAK3/STAT3 pathway in susceptibility to NSCLC development. It should be stressed that correlation between increased STAT3 gene expression and TT genotype (rs3816769) of the STAT3 gene in our patients may be useful in future diagnosis of NSCLC risk in the Polish population. However, further studies are needed on a larger group to draw firm conclusions.

Acknowledgments The study was funded by a grant from the Ministry of Science and Higher Education (grant no. 502/03-1-151/04/502-14-069).

REFERENCES


Polimorfizm genu STAT3 rs3816769 wiąże się z poziomem jego ekspresji i może sprzyjać rozwojowi niedrobnokomórkowego raka płuc – badanie wstępne

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STRESZCZENIE

Wprowadzenie Gen STAT3 pełni funkcję zarówno onkogenu, jak i regulatora odporności. Pomimo jego istotnej roli w rozwoju raka i regulacji komórek układu immunologicznego, nieliczne są badania polimorfizmów pojedynczego nukleotydu (single nucleotide polymorphism – SNPs) genu STAT3 i związanego z tym ryzykiem wystąpienia raka płuc.

Celem W tym badaniu oceniano związek między SNP (rs744166 [AG] i rs3816769 [CT]) a predyspozycją do rozwoju NSCLC oraz ich potencjalny wpływ na ekspresję STAT3.

Pacjenci i metody DNA i RNA zostało wyizolowane od pacjentów z rozpoznanim NSCLC (n = 71) oraz od osób bez rozpoznania nowotworu, zakwalifikowanych do grupy kontrolnej (n = 104). Do genotypowania SNP genu STAT3 oraz do badania ekspresji użyto sond TaqMan®.

Wyniki STAT3 CC (rs3816769) oraz AA (rs744166) genu STAT3 były związane z mniejszym ryzykiem występowania nowotworu płuc, podczas gdy genotypy TT (rs3816769) i GG (rs744166) mogą je znacznie zwiększać. Analiza ilorazu szans (odds ratio) wykazała, że allele A może zmniejszać ryzyko NSCLC, natomiast allele G może to ryzyko zwiększać. Wykazano, że nadmierna ekspresja STAT3 dodatnio koreluje z genotypem TT (rs3816769) u chorych na NSCLC (p = 0,0464). Ponadto zaobserwowano różnice w ekspresji genu STAT3 między rakiem płaskonabłonkowym a rakiem wielkokomórkowym.

Wnioski Wykazano, że polimorfizm rs3816769 genu STAT3 oraz różnice w poziomie jego ekspresji są związane z wrażliwością na NSCLC i mogą mieć duże znaczenie funkcjonalne oraz istotną wartość diagnostyczną.