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Fucosylation of serum glycoproteins in lung cancer patients

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Abstract

Increased expression of sialyl Lewis X or A antigens on metastatic cancer cells leads to their selectin-mediated extravasation. Profound fucosylation of the serum microenvironment may be a factor that interrupts adhesion and influences the formation of metastases. In this study we quantitatively analyzed fucosylation of serum glycoproteins in small-cell and non-small-cell lung cancer patients. Fucosylation of four chosen glycoprotein bands was measured as the reactivity with *Aleuria aurantia* lectin on nitrocellulose blots, preceded by polyacrylamide gel electrophoresis. Relative fucosylation and fucosylation coefficients were calculated by densitometric analysis. Fucosylated oligosaccharides were observed in higher amounts in cancer sera when compared to sera from healthy individuals in all bands analyzed. Glycoproteins of a molecular mass of 29 kDa appear to carry more fucose residues than the 42-kDa band, comprising α_1-acid glycoprotein and haptoglobin. Glycans of the 26-kDa band were fucosylated to a higher extent in non-small-cell vs. small-cell lung cancer. The results suggest that the extent of fucosylation could be a useful marker for estimation of the glycosylation status of serum proteins in cancer patients. Cluster analysis leads to the preliminary suggestion that the fucosylation status could serve as a predictive factor for patient survival.

Keywords: *Aleuria aurantia* lectin; carbohydrate ligands; fucosylation; lung cancer; metastasis.

Introduction

Most of the proteins essential for proper cell function are glycosylated. Carbohydrates are now considered to be molecules possessing enormous potential for encoding biological information. They may serve as cellular identification tags through which cells can interact with their surroundings (1, 2). Glycan modifications can confer unique functional properties on oligosaccharides and are strictly regulated during ontogeny and cellular differentiation (3). Aberrant glycosylation lies in the background of numerous diseases and in other cases may result from the pathological events (4–6). The diversity of carbohydrate structures results in a great complexity of possible alterations, among which a great deal of interest has been focused on the expression of the terminal monosaccharides, sialic acid and fucose (7–9).

One of the best-studied functions of fucose is its role as an essential component of the carbohydrate ligands for the selectin family of cell adhesion molecules (1, 8, 10, 11). These interactions are essential for proper recruitment of neutrophils and T-cells to inflammatory sites and lymphocyte trafficking to secondary lymphoid organs (12). Similar interaction is crucial for the progress of cancer. Cancer cells, released to the blood from the primary tumor, often overexpress sialylated and fucosylated glycans on their surface. Their interaction with endothelial selectins mimics the inflammatory adhesion cascade, initiating extravasation, colonization of new tissues and the formation of secondary tumors (1, 8, 10, 11).

Since it was found that soluble oligosaccharides or glycopeptides have the ability to interfere with carbohydrate-protein interaction, attempts have been made to apply such compounds as specific competitive inhibitors of this process to restrict the invasiveness of cancer (13–15). This novel and promising approach to therapeutic intervention draws attention to the fact that blood plasma provides an environment rich in fucosylated glycans. It has been confirmed that in numerous, mainly inflammation-associated diseases the carbohydrate structure of acute-phase proteins is altered (16). Nascent sugar epitopes, for example sialyl Lewis X (sLeX), mimic those involved in the recognition process prior to extravasation of neutrophils and invasive cancer cells. Therefore, such glycans of circulating glycoproteins could act as natural endogenous inhibitors of inflammation or metastasis (17). The ability to synthesize such sugar epitopes may be of predictive importance for the patient.

Glycosylation (fucosylation and sialylation) analyses of serum proteins have most often focused on one glycoprotein, usually acid α_1-glycoprotein (AGP) (18, 19). Information as to whether alterations in AGP glycans are representative of the other circulating glycoproteins is limited. In this study we attempted to estimate the amount of fucosylated sugar epitopes expressed on different serum glycoproteins of lung

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cancer patients. We aimed to determine if any of these serum proteins can serve as a special carrier of fucosylated glycans and if such overexpression may be associated with a type or stage of the cancer.

Materials and methods

Clinical subjects

A total of 29 (Nos. 1–29) patients with pathologically documented lung cancer, treated in the Department of Pulmonary Diseases, Wrocław Medical University, were consecutively recruited to the study for a 1-year period. All serum samples were collected before treatment (surgery or chemotherapy). Thoracic computed tomography was used to stage the disease. In operable patients, surgical tumor, lymph node involvement, and metastasis (TNM) staging was done. Ultrasonography of the abdomen was carried out to estimate upper abdominal metastatic disease. The patients were divided into two distinct groups:

a) There were 18 patients (Nos. 1–18) diagnosed with non-small cell lung cancer (NSCLC) at different stages of cancer development: I, 11.5% (Nos. 9 and 13); IIIA, 5.5% (No. 16); and IV, 44.5% (Nos. 1, 3, 6, 7, 10, 11, 12, and 18). Seven patients had inoperable tumors at the time of diagnosis, so classification using the TNM system was not carried out (Nos. 2, 4, 5, 8, 14, 15, and 17). During the course of our study, six patients (33%) died after an average of 4.4 months from the time of the diagnosis (Nos. 1, 3, 6, 10, 15, and 16). There were four adenocarcinomas, five cases of squamous carcinoma, one large clear-cell cancer, and eight cases of undifferentiated cancer included in this group.
b) There were 11 patients (Nos. 19–29) diagnosed with small-cell lung cancer (SCLC). For seven of them (Nos. 19, 21, 22, 23, 24, 26, and 29, i.e., 64%) the stage of the disease was confirmed to be extensive, as hepatic and adrenal metastases were observed. Three of them died during the course of our study.

All experiments in this study were performed with respect to a control group. Serum samples of 40 healthy blood donors with routine blood test results within the physiological range were pooled and used as a reference serum (RS).

Of the 40 serum samples from healthy subjects, 10 were randomly chosen and considered as a control group (Nos. 30–39).

Sodium dodecyl sulfate-polyacrylamide gel (SDS-PAGE) and Western blotting

Electrophoresis was performed in polyacrylamide (100 g/L) gels according to Laemmli (20). Serum samples were prepared by heating for 8 min at 100°C with sodium dodecyl sulfate (SDS; 10 g/L) and β-mercaptoethanol (22.3 g/L). Samples of 0.75–3.5 μg of total serum protein were loaded onto the gel lanes in experiments to standardize the method, and 2.5 μg per lane was used for analysis of the reactivity with *Aleuria aurantia* lectin (AAL). Two identical gels were developed simultaneously; one of them was silver-stained (21) and the other was transferred onto nitrocellulose according to the standard procedure (22). Nitrocellulose sheets were blocked overnight with Tween (10 g/L) in Tris-buffered saline, pH 7.4 (TBS), and then probed with AAL. RS was developed in every gel.

Aleuria aurantia lectin reactivity

Fucosylation of serum glycoproteins was analyzed based on their reactivity with fucose-specific AAL (23). Blots were incubated with biotinylated AAL (4 mg/L; Vector, Burlingame, CA, USA) for 1 h at 37°C. Washing the excess lectin (4× TBS-Tween, 1 g/L) was followed by incubation with extravidin-alkaline phosphatase conjugate (Sigma, St Louis, MO, USA; 1:5000) for 1 h at 37°C and another extensive wash. Lectin-glycoprotein complexes were visualized by alkaline phosphatase reaction, with nitroblue tetrazolium and 5-bromo-4-chloro-3-indolyl phosphate as the substrates.

Densitometric analysis

Silver-stained gels and blots probed with AAL were scanned with a Plustec OptiPro scanner (Plustec Inc., Taipei, Taiwan) and analyzed with Scion Image (Macintosh Package) software (Scion Corporation, Frederic, Maryland, USA) for densitometric analysis. The relative protein content in each band analyzed was expressed as the ratio of this band's optical density (OD) to the OD of the respective band for RS in silver-stained gels. Relative fucosylation of an individual band was similarly estimated as the ratio of the OD of this band to the OD of the respective RS band, both measured on AAL-probed blots, similarly to the calculations applied by Rydén et al. (24).

Statistical analysis

Statistica 5.0 software (StatSoft Poland Ltd., Kraków, Poland) was applied for the basic statistical analysis. Correlation between the variables was tested with the Pearson correlation coefficient. To analyze variations in the fucosylation coefficients in different groups of patients, the Mann-Whitney U-test was used. We applied a non-parametric test instead of the t-test, since the sample size was not large and did not fulfil the requirements for parametric statistical analysis.

Cluster analysis

In cluster analysis each of the 39 subjects was represented by a vector of eight features, i.e., the relative amounts of protein and fucose in the 77-, 42-, 29- and 26-kDa bands, in the eight-dimensional vector space. The similarities between the points were calculated using different clustering parameters, including different metrics (euclidean, Manhattan city block, and Canbery), on the original data points, as well as the scaled points (25, and references therein). The mean values for each point in the cluster were calculated as the mean average or weighted mean average (procedure A).

The analysis was repeated for all 39 subjects represented by a vector of four features defining the relative fucose amount (procedure B). In another experiment, the 39 subjects were defined by a vector of two features representing two principal components and calculated using a standard procedure of the Statgraphic software package (Manugistic Inc., Rockville, Matyland, USA). These components contained 67% of the information from the original data, as indicated by the sum of their eigenvalues (procedure C).

Results

Electrophoresis of cancer and normal sera was simultaneously developed on two gels as described in

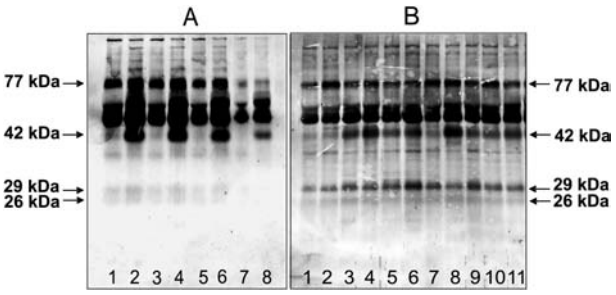

Figure 1 Lectin-blot analysis of serum glycoproteins. After SDS-PAGE, serum samples were transferred to nitrocellulose and probed with *Aleuria aurantia* lectin. (A) Standardization procedure: odd lanes, reference serum (RS); even lanes, cancer serum (No. 6). Loading: lanes 1 and 2, 3.50 μg; 3 and 4, 2.62 μg; 5 and 6, 1.75 μg; 7 and 8, 0.75 μg of total serum protein. (B) Serum samples: lane 1, RS; lanes 2–6, NSCLC; lanes 7–11, SCLC.

Materials and methods. One electrophorogram of each pair was silver-stained and corresponded to the amount of protein in the sample studied, whereas the second one was transferred to nitrocellulose and treated with the lectin from *Aleuria aurantia*, which indicates the amount of fucose (Figure 1).

After visual estimation of the electrophoretic patterns, four different bands were selected for further studies, as they showed the most significant differences between normal and cancer sera and were well separated for band scanning. These bands represented proteins of 77, 42, 29, and 26 kDa.

Standardization

It was assumed that the integrated OD of the bands corresponded to the amount of protein (silver-stained) and fucose (based on their reactivity with AAL). In order to check linearity between the protein and fucose amounts and the integrated OD, two chosen sera were submitted to electrophoresis (RS and one cancer serum sample) in four different amounts: 3.5, 2.62, 1.75, and 0.75 μg of total serum protein per lane (Figure 1A). The regression analysis showed good linear dependence of the OD values on the sample amount up to 2.62 μg of protein for both protein and fucose. The correlation coefficients for all protein and fucose bands were equal to 0.995 or higher. Thus, in all further experiments 2.5 μg of total serum protein was loaded onto gel lanes.

Fucosylation coefficients

To measure the degree of fucosylation of particular proteins, the variation in fucosylation coefficients within the subject groups studied was analyzed. The relative fucosylation coefficient was defined as the ratio of the relative amount of fucose to the relative protein amount in each band analyzed, which was calculated using the following formula:

$$F_R = \frac{F_{(x)}}{P_{(x)}} = \frac{OD_{AAL(x)}/OD_{AAL(RS)}}{OD_{prot(x)}/OD_{prot(RS)}}$$

The mean values for the fucosylation coefficients are presented in Table 1, and their distributions in whisker-and-box diagrams in Figure 2. The diagrams show the quartile distribution of fucosylation coefficients of each group of patients in particular protein bands. Differences in the distribution of fucosylation coefficients between cancer patients and healthy subjects were observed in all except the 42-kDa band. In healthy subjects the fucosylation coefficients for all glycoproteins studied were close to 1, in accordance with our expectations. In both SCLC and NSCLC patient groups, the mean fucosylation coefficients increased in all four bands analyzed compared to the healthy reference group. The quantitative increase in the average fucosylation coefficient was similar for both types of cancer and ranged from 15–20% in the 77-kDa band to 45–48% in the 29-kDa band.

To check whether the variation in fucosylation coefficients was statistically significant between healthy subjects and cancer patients, as well as between patients with two different types of cancer, we performed Mann-Whitney U-tests for each pair of fucosylation coefficients calculated for all the protein bands studied. As shown in Table 2, the differences between the fucosylation coefficients were statistically significant for all proteins studied when healthy and NSCLC patients were compared, and only for low-molecular-mass proteins (29 and 26 kDa) when healthy and SCLC patients were compared. No statistically significant differences in fucosylation coefficients were found between SCLC and NSCLC patients for all proteins studied.

Correlation analysis of the protein amount and fucosylation level

In cancer sera, increased fucosylation follows the acute-phase reaction. Thus, to compare the dynamics of both processes, correlation between the protein and fucose contents was calculated for all bands studied (77, 42, 29, and 26 kDa), and all 39 sera. The correlation coefficients and their confidence intervals are presented in Table 3. All statistically significant correlations are marked in bold font. For healthy sub-

Table 1 Mean values of fucosylation coefficients with standard deviation.

Subject group	Band			
	77 kDa	42 kDa	29 kDa	26 kDa
Control, n = 10	1.041 ± 0.12	0.835 ± 0.24	1.138 ± 0.68	1.090 ± 0.38
SCLC, n = 11	1.166 ± 0.29	1.103 ± 0.34	2.076 ± 0.46	1.656 ± 0.47
NSCLC, n = 18	1.223 ± 0.26	1.238 ± 0.36	2.180 ± 0.55	1.518 ± 0.36

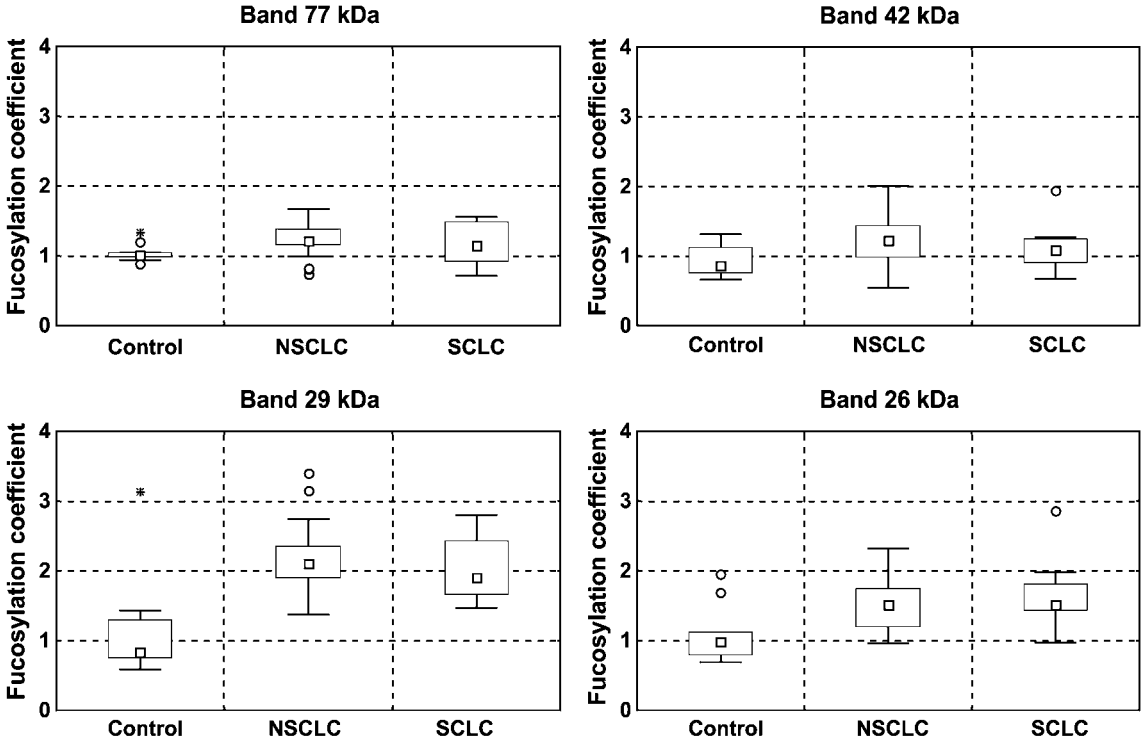

Figure 2 Distribution of the fucosylation coefficient (F_R) values in healthy and cancer subjects. Frames represent results within 25–75%; bars min/max of nonoutliers; □ median; ○ outliers; ∗ extreme.

Table 2 Statistical significance in Mann-Whitney U-tests for fucosylation coefficient.

Group comparison	Band			
	77 kDa	42 kDa	29 kDa	26 kDa
Vs. control group (n=10)				
SCLC (n=11)	0.398	0.307	**0.0019**	**0.0124**
NSCLC (n=18)	**0.0415**	**0.0188**	**0.0006**	**0.0084**
Vs. NSCLC (n=18)				
SCLC (n=11)	0.621	0.234	0.621	0.620

Statistically significant values are given in bold.

jects, correlation between the protein amount and the fucosylation level was weak or even very weak. The highest positive correlation coefficients were found for SCLC patients (ranging from 0.748 to 0.907), with slightly lower values for NSCLC patients (ranging from 0.521 to 0.785) for proteins of 42, 29, and 26 kDa. For NSCLC patients, the correlation calculated for the 29-kDa band (0.360) was moderate, but its confidence interval was too high to treat it as statistically significant. For the protein of 77 kDa, the correlation was weak or very weak and was negative for all three groups of subjects.

Cluster analysis

For more detailed insight into the significance of fucosylation, three different clustering analyses were performed, described in the Materials and methods section. We aimed to analyze cancer types, their stage and prognosis for subjects classified into particular clusters.

All three procedures divided the subject groups, analyzed in a similar way, into four separate clusters, and individuals who did not belong to any of the four clusters (cluster V). Data for cluster analysis are summarized in Figure 3.

As an example, a dendrogram obtained with procedure B is shown in Figure 4. Analysis of the dendrogram showed four distinct clusters and four individual cases who did not belong to any of the clusters. The latter were gathered as cluster V. The number of patients from each group (NSCLC, SCLC, control) and the percentage of them in each cluster are summarized in Table 4. Analysis of the Table indicates that 90% of healthy people were classified into cluster I, with 63% of NSCLC patients classified into clusters III and IV, whereas SCLC patients were randomly distributed in all five clusters.

Using procedure B, cluster I grouped mainly healthy persons from the control group. For cancer patients, classification into this cluster is connected with relatively good prognosis: in the course of our

Table 3 Correlation between the amount of protein and fucose in serum glycoproteins analyzed.

Subject group	Band			
	77 kDa	42 kDa	29 kDa	26 kDa
NSCLC, n = 18	−0.127 ± 0.454 Weak	**0.521 ± 0.336** **High**	0.360 ± 0.402 Moderate	**0.785 ± 0.177** **Very high**
SCLC, n = 11	−0.317 ± 0.531 Moderate	**0.840 ± 0.174** **Very high**	**0.748 ± 0.260** **Very high**	**0.907 ± 0.105** **Very high**
Control, n = 10	−0.187 ± 0.598 Weak	0.206 ± 0.593 Weak	0.052 ± 0.618 Very weak	0.213 ± 0.591 Weak

Statistically significant values are given in bold.

study only one such patient died. In spite of the presence of distant metastases, the survival time was 16 months. Cluster II exclusively grouped patients with advanced disease, numerous distant metastases and poor prognosis. All patients in this group died a short time after diagnosis (average 3 months). Classification into clusters IV and V is connected with good prognosis; for <30% of patients the survival time was approximately 1 year and >70% of them were still alive at the end of our analysis.

In classification C, cluster I grouped 90% of healthy individuals. This group also included the same SCLC patient who survived for 16 months grouped into cluster I in the previous clustering procedure (B). Classification into cluster V correlated with good prognosis. None of the patients from this cluster died in the course of our study. Clusters II–IV grouped patients with worse prognosis: 50% of them died after an average of 6 months after diagnosis. Surprisingly, cluster IV included one person from the reference group. In spite of normal values of routine hematological examination, we cannot exclude the existence of undiagnosed somatic disease in this case.

Discussion

The role of fucosylated carbohydrate structures in cell-cell and cell-matrix interactions has been confirmed in numerous studies (10). This monosaccharide, located in a terminal position and therefore exposed to the environment, directly participates in interactions with specific receptors and adhesive molecules.

Cancer cells exploit the ability to alter the pattern of their surface glycans to escape from the control of the immunological defense system while circulating in blood, and this is essential for their extravasation. Elevated levels of fucosylated epitopes on the surface of cancer cells were shown to increase their metastatic potential and ability to colonize new tissues (5, 26–28). Overexpression of sialylated and fucosylated glycans is connected with poor prognosis in numerous types of human cancers, such as colorectal, gastric, breast, urinary bladder and lung adenocarcinoma (10). The mechanism of participation of sLeX antigens in metastasis is still not sufficiently described, although its complexity is not in doubt. Apart from direct interaction of the surface glycans of cancer cells with endothelial E-selectins, which leads directly to extravasation, metastasis also includes thromboembolization as a result of sLeX interaction with platelet P-selectins, as well as limited tumor infiltration by lymphocytes (10, 11, 29).

Many efforts concern the designation of specific inhibitors acting in situ, such as simple or complex carbohydrate structures (10, 13–15). However, aiming to diminish the pathological interaction with exogenous oligosaccharides, we seem to neglect the fact that a circulating cancer cell is suspended in an environment of profound fucosylation. These fucosylated structures include the oligosaccharide moiety of circulating glycoproteins. The other possible partners of complex interactions are soluble forms of adhesive molecules, shed from the endothelial cells and leukocytes, which can serve as specific receptors for carbohydrate epitopes. These multivalent factors may form a complicated net of interacting factors probably important in predicting cancer metastases (30–32).

Most of the information concerning the increase in fucosylation of circulating glycoproteins obtained so far is qualitative. Detailed quantitative studies were limited to AGP and haptoglobin (18, 19, 33). The development of acquisition systems and computational techniques allowed us to attempt the complex quantitative analysis of glycoprotein fucosylation in sera of lung cancer patients. An increase in fucosylated glycans in NSCLC sera was recently reported by Otake et al. (34). The authors did not attribute the increased oligosaccharides to any particular protein carrier; the oligosaccharide pattern of the sera analyzed was not compared to SCLC and other possible pathologies. The correlation of serum levels of sLeX antigens with distant metastases in NSCLC was reported by Satoh et al. (35). Moreover, high levels of the sLeX antigen correlated significantly with poor survival. Determination of serum sLeX levels can be used as an adjunctive diagnostic marker; however, it also increases in some non-malignant diseases, such as idiopathic pulmonary fibrosis (IPF) (36). Comparing Western blots of patient sera developed with anti-sLeX antibodies, Satoh et al. found significant differences in the electrophoretic patterns between IPF and lung carcinoma, especially in bands of high molecular weight. Although we did not observe significant fucosylation changes in high-molecular-weight bands (>100 kDa) in our patients, further characteristics of serum glycosylation in lung cancer patients, compris-

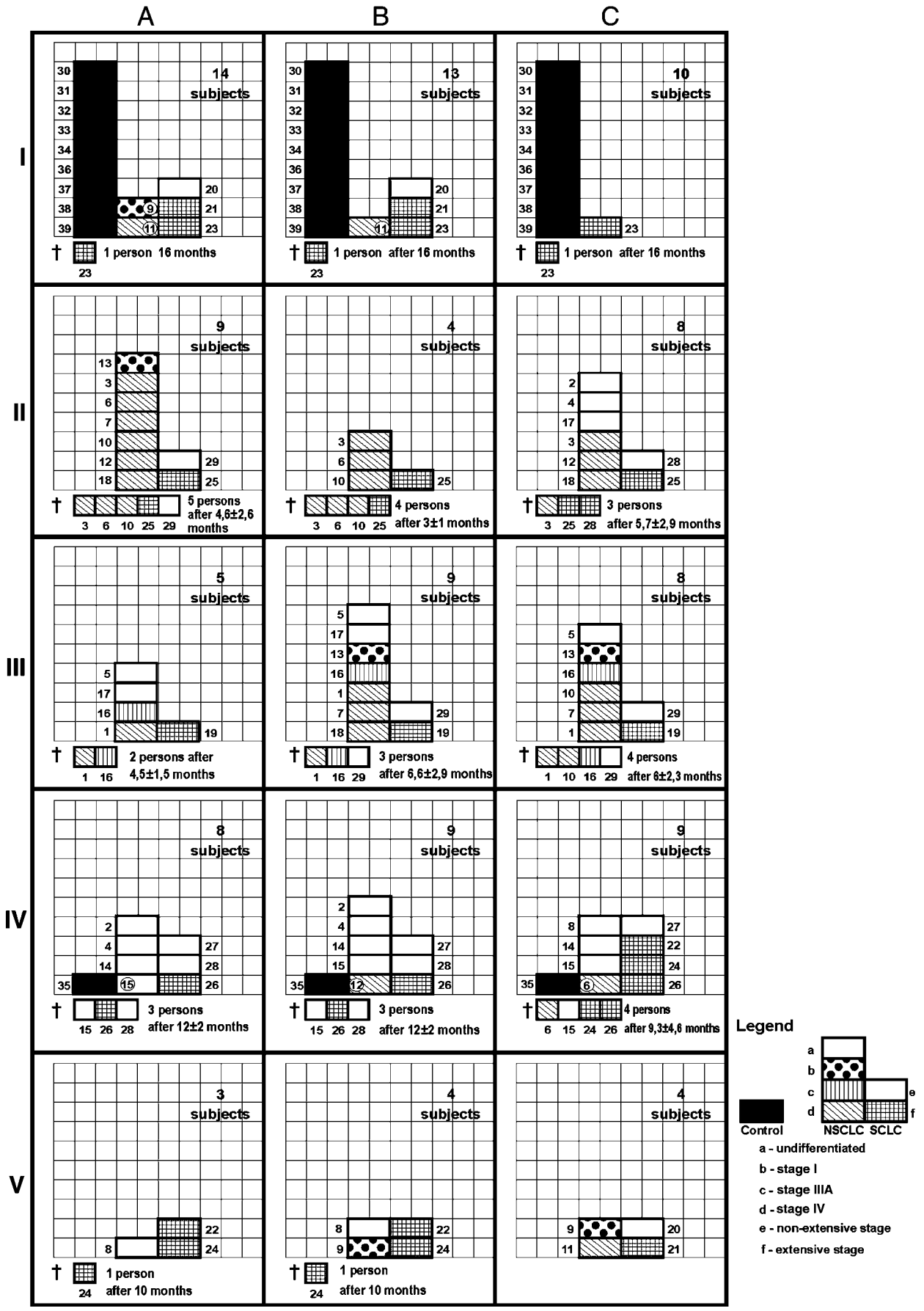

Figure 3 Cluster analysis for healthy and cancer subjects. In three procedures used for calculations the subjects were represented as follows: (A) vector of eight features: relative protein and fucose in bands at 77, 42, 29, and 26 kDa; (B) vector of four features: relative amount of fucose in bands at 77, 42, 29 and 26 and (C) vector o two features representing the first two principal components containing 67% of the information from the original data. Nos. 1–18, NSCLC; 19–29, SCLC; 30–39, control group.

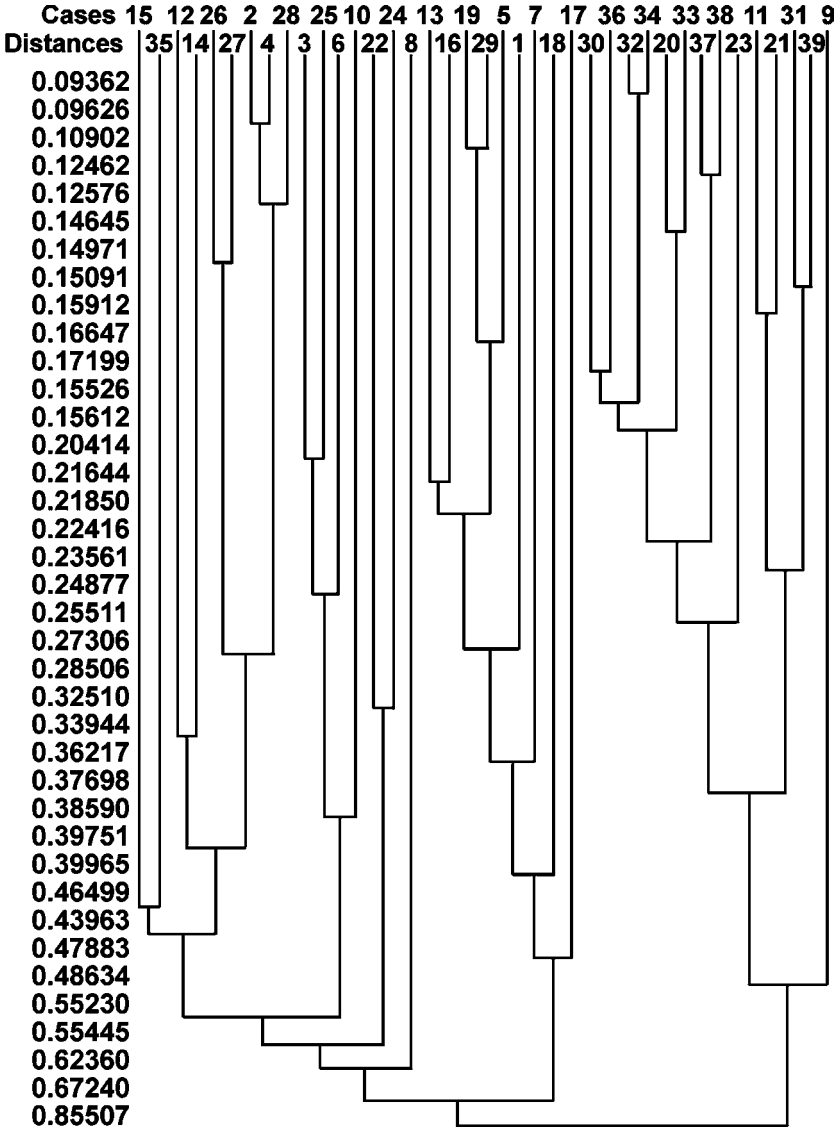

Figure 4 Dendrogram of cluster analysis of the healthy and cancer subjects. In the procedure referred to as 'B' in the text each subject was represented by a vector of four features: relative amount of fucose in bands at 77, 42, 29, and 26 kDa, measured as the reactivity with *Aleuria aurantia* lectin. Nos. 1–18, NSCLC; 19–29, SCLC; 30–39, control group.

ing both fucosylation and sialylation, may help to establish diagnostic or prognostic carbohydrate markers. The advantage of simultaneous and comprehensive examination of the expression of numerous proteins, as well as their glycosylation, is now possible using proteomics and glycomics techniques. These methods, although precise and highly resolving, are still characterized by some interpretative problems originating from normal biological variability, which therefore limit the analysis of individual samples (37, 38). Treating the current study as an introduction to wider glycomic analysis, we also aimed to gain insight into the individual variability of features analyzed in healthy and ill subjects.

The total amount of fucose, measured as an integrated OD in blots probed with AAL and summarized for four bands, almost doubled in the sera of cancer patients. These alterations accompany the typical acute-phase reaction, manifested by changes in the amounts of protein carriers subjected to fucosylation. Thus, for the positive acute-phase proteins (band 42 kDa) the fucosylation coefficient, defined as the

Table 4 Number of cases classified into particular clusters.

Subject group	Cluster number				
	I	II	III	IV	V
Control	9 (90.0%)	0	1 (10%)	0	0
NSCLC	1 (5.3%)	0	7 (36.8%)	5 (26.3%)	2 (10.5%)
SCLC	3 (27.3%)	1 (9.1%)	2 (18.2%)	3 (27.3%)	2 (18.2%)

The percentage with respect to the whole group is given in parentheses.

ratio of the amounts of fucose and protein, increased only 1.5-fold. For the 77-kDa band, containing the negative acute-phase protein transferrin, the total amount of fucose slightly increased, in spite of the decrease in protein content. It is worth noting that transferrin, having only two glycosylation sites, is evidently a less effective carrier of carbohydrate epitopes. AGP, containing five glycan chains, and haptoglobin, with its four oligosaccharides in every β-subunit, seems to be more efficient. In addition, the highly polymeric structure of haptoglobin offers a higher density of multivalent carbohydrate epitopes, which is considered necessary in this type of interaction. The high correlation of protein and fucose content for the 42-kDa band suggests that the degree of fucosylation keeps pace with the increasing amount of protein carrier. This can play an important role in providing sufficient carbohydrate content in the microenvironment of the blood.

Individual variability of fucose expression is significant. This is not surprising, considering the high diversity of the groups studied with respect to type and stage of the disease. In the analysis of the distribution of fucosylation coefficients, we paid some attention to outlying points, i.e., those lying outside the four quartiles of distribution. There were seven cases of such cancer patients; in every one of them fucosylation changes were limited to one out of the four bands analyzed. In three of these cases with very short survival times, fucosylation of the 77-kDa band was significantly decreased. The other outliers showed increased fucosylation in one of the other bands. Most of outliers were observed for subjects with advanced cancer development. However, outlying cases were also observed in the control group of healthy subjects.

Cluster analysis divided patients into groups that did not reflect the type of cancer and its development, but rather prognosis towards the further course of disease. Procedures based on fucosylation and eliminating the effect of correlation between protein and fucose content (B and C) were more efficient for clustering than using independent data on fucose and protein content (procedure A). In the cluster grouping patients with the worst prognosis (B II) the highest increase in the amount of fucose was observed for the 42-kDa band, containing AGP and haptoglobin. This observation confirms that both proteins are efficient carriers of fucosylated glycans. Relative fucosylation, expressed as the fucosylation coefficient, increased mainly in the 29-kDa band, in which fucose overexpression was not preceded by any increase in the amount of protein. Transferrin (77-kDa band) fucosylation in this cluster did not increase.

In the group of patients with the best prognosis (C V) fucose content mainly increased in the 26-kDa band, and the fucosylation coefficient (relative fucosylation) in the 29-kDa band.

The usefulness of tumor markers in the diagnosis of lung cancer, especially NSCLC, is not well defined. Knowledge of pretreatment prognostic factors would be helpful in selecting the most suitable therapy and predicting the probable course of the disease (36, 39, 40). Our data, although obtained for small groups of subjects, demonstrate that in the sera of lung cancer patients, overexpression of fucosylated glycans differs among particular glycoproteins, as well as in cancer types. The glycosylation mechanism follows the increased synthesis of acute-phase proteins, providing a high number of fucose-containing epitopes. The insufficient quantity of subjects investigated limits any inference on the role of elevated fucosylation. The preliminary data for cluster analysis presented here, although promising, need to be confirmed in further studies, which should enroll a greater number of patients and follow them up for a longer period. Such results of higher statistical relevancy will also give an insight into the possible connections between fucosylation, the histopathological characteristics of cancer and its clinical stages. It seems that the general fucosylation pattern of serum proteins may be promising in the search for factors of prognostic value.

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