

## Proteomic and glycomic investigation of ALK rearranged lung tumor samples

Mirjam Balbisi<sup>1</sup>, Gábor Tóth<sup>1</sup>, Simon Sugár<sup>1</sup>, László Drahos<sup>1</sup>, Gitta Schlosser<sup>2</sup>, Judit Moldvay<sup>3</sup>,  
A. Marcell Szász<sup>3,4</sup>, Lilla Turiák<sup>1</sup>

<sup>1</sup>ELKH Research Centre for Natural Sciences, MS Proteomics Research Group, Budapest, Hungary

<sup>2</sup>MTA-ELTE Lendület Ion Mobility Mass Spectrometry Research Group, Budapest, Hungary

<sup>3</sup>National Korányi Institute of Pulmonology, Budapest, Hungary

<sup>4</sup>Semmelweis University, Budapest, Hungary

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Lung cancer is one of the most common types of cancer responsible for the most cancer-related deaths. Proteoglycans play important regulatory roles in the extracellular matrix, the balance of which is disrupted in many cancers. Thus, we analyzed the proteomic and glycosaminoglycan composition of lung tissues carrying ALK translocation, belonging to the group of non-small cell lung cancer. A total of 22 regions on seven tissue sections were examined by nanoUHPLC-MS/MS measurements after tryptic, heparin lyase, and chondroitinase ABC digestion, respectively. Sample group comparisons based on pathological classification (e.g. solid, tubular or papillary tumor) will be shown.

We detected 317 proteins showing altered expression between different sample groups. A large portion of proteins that vary significantly between tumor types were involved in the regulation of protein synthesis. Proteins that were found to be differentially expressed between adjacent normal and distinct tumor sample groups are involved in several important biological processes as well, such as the organization of the extracellular matrix.

The differences between the individual samples were examined by statistical hypothesis testing, principal component analysis and hierarchical clustering. In the principal component analysis, adjacent normal tissue regions were separated from tumor samples in all cases and a considerable number of the solid tumor and papillary tumor samples were also separated.

The glycomic investigations were interpreted based on the total amount and the sulfation patterns of chondroitin-sulfate (CS) and heparan-sulfate (HS) disaccharides. Compared to the adjacent normal tissue regions, increased CS and HS content was observed in all tumor sample groups; the mean sulfation also increased. The ratio of CS disaccharides sulfated at the 6-*O* position compared to those sulfated at the 4-*O* position was slightly reduced as well as the *N*-sulfation of HS in the tumorous regions compared to adjacent normal regions. The three tumor types showed the largest differences in the total amount of HS chains.

The identified qualitative and quantitative changes give an excellent starting point for further targeted biomarker research based on proteoglycans.