

LC-MS/MS analysis of protein biomarkers diagnosing Small Cell Lung Cancer in human serum

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In this paper the ongoing research for determination of (very) low abundance protein biomarkers in human serum using LC-MS/MS for Small Cell Lung Cancer (SCLC) is presented.

SCLC is an aggressive disease with rapidly growing neoplasm. This cancer is highly sensitive to systemic chemotherapy, but may have disseminated before diagnosis is made. This call for a sensitive, reliable and rapid method of diagnosis in order to initiate proper treatment at an early stage. Additionally, methods like these are of great value in monitoring the treatment.

At the present time, protein biomarkers which indicate SCLC are, among others, ProGRP, NSE and CEA. Reference values for these diagnostic proteins in human serum in healthy subjects vary from pg/mL (ProGRP) to ng/mL (NSE and CEA) levels. In case of pathology, the concentrations of these biomarkers are elevated in serum. To determine their concentrations ELISA and RIA are used. Although good detection limits are reached, they are non-automated, labor intensive and susceptible to cross-reactivity. Such problems can be avoided using LC-MS/MS.

Data from LC-MS/MS experiments of ProGRP are used here to show the strategy of determining protein biomarkers in human serum. Aspects like sample digestion and selection of biomarker-specific proteolytic products with subsequent tandem MS characterization will be discussed. Attention is paid to various steps for sample preparation and clean-up ranging from non-specific (MeCN precipitation) to highly specific (immuno-capture). Their impact on the quantitative determination is shown. The performance of the whole analysis method is evaluated and its applicability on clinical relevant samples presented.