

IDENTIFICATION OF NON-SMALL CELL LUNG CANCER BIOMARKERS USING MASS SPECTROMETRY

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With the completion of the human genome sequence, the biomedical sciences have entered in the “omics” era. This has been mainly due to the development of high-throughput genomic techniques, such as microarrays and, in recent days, the application of mass spectrometry to proteomic analysis. However, there is still a gap between these technological advances and their direct application in the clinical setting. The work hereby presented is designed to build bridges between high-performance proteomics and clinical routine.

Protein extracts were obtained from clinical non-small cell lung cancer (NSCLC) samples. Using a phosphopeptide enrichment-based approach, we performed proteomics analyses based on high resolution mass spectrometry, using an LTQ-Orbitrap XL mass spectrometer (Thermo Scientific). Subsequent ontological analyses and label-free quantification using SIEVE software (Thermo Scientific) were carried out. Some of the identified biomarkers were validated using classical proteomics techniques. Results were analyzed using several statistical approaches.

Our results show that it is possible to discriminate normal from tumor tissue and between different subtypes of NSCLC using LC-MS/MS. With this technology we were able to assess protein and phosphoprotein patterns on these samples, identifying dozens of differential markers between normal and tumor tissue, and some markers that discriminate between adenocarcinoma and squamous cell carcinoma, the two most common histological subtypes of NSCLC. Gene Ontology analyses performed show great potential identifying signaling pathways and biological processes susceptible of therapeutic intervention, and may provide clues to the genesis of the disease and underlying molecular alterations.

The requirement of a molecular test that complements the classic clinical diagnosis of lung cancer has been pinpointed by the results of recently developed clinical trials, demonstrating different response patterns to specific drugs according to histological subtype. The application of discovery-based proteomics analyses in clinical samples allows us to identify new biomarkers and new potential therapeutic targets in NSCLC.