PROTOMIC APPROACH TOWARD BIOMARKER DEVELOPMENT FOR DIFFERENTIAL DIAGNOSIS IN MALIGNANT PLEURAL MESOTHELIOMA

Y. Sugihara, K. Mukaihara, T. Kondo

Division of Pharmacoproteomics, National Cancer Center Research Institute, Tokyo, Japan

[Backgrounds] Malignant pleulra mesothelima is one of the most deadly malignancies (MPM), and novel findings to improve therapeutic strategies have long been desired for clinical proteomics. There are critical needs for differential diagnosis between MPM and lung adenocarcinoma (LA) in clinical scenes, because symptons of the two diseases are overlaped at the early stage and their therapeutic regimens are quite different. As pleural effusion (PE) is one of the most common early symptons in these diseases and PE are obtained by low-invasive methods, PE can be considered a source of biomarkers for differential diagnosis. [Purpose] We aimed to identify the PE proteins that can be biomarker candidates for differential diagnosis between MPM and LA. [Materials and methods] This study included the PE samples from four MPM patients and four LA ones. Proteins in these PE samples were firstly separated according to molecular weight by SDS-PAGE. Then the fractionated proteins were recovered into 24 gel pieces manually. The proteins were were extracted from the gel pieces as peptides by in-gel digestion method with trypsin. The peptides were subjected to mass spectrometry (LTQ, Thermo scientific). The relative amount of peptides was measured by spectral count and integrated with molecular weight data by PROTOMAP software [1]. The functional classification of identified proteins was performed based on the Gene Ontology using Database for Annotation, Visualization and Integrated Discovery (DAVID) (http://david.abcc.ncifcrf.gov/). [Results] We observed 230 and 267 unique gene products in the PE samples from the MPM and LA patients, respectively. Comparative expression study resulted in the identification of 97 proteins (MPM; 67 proteins, LA; 30 proteins). According to the functional annotations, these identified proteins may play important roles in signal transduction, development and proteolysis. These identified proteins included those with unexpected molecular weight, and such proteins may have novel biological properties in PE. The proteins correlated with malignancies were also included in these identified proteins. [Conclusions] We examined the protein contents in PE from the patients with MPM or LA. The proteins which exhibited differential expression between these two dieseases and had functional significances in malignant phenotypes may have the clinical utilities as biomarkers for differential diagnosis.

Reference

1. M. Dix, G. Simon, B. Cravatt; Cell, **134**, 679-691 (2008)