Can proteomics lead to the discovery of real biomarkers for HCC?

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Abstract

The development of proteomics technologies has lead to a great deal of effort being focused on the identification of biomarkers for cancers. Although many papers have reported candidate biomarkers for hepatocellular carcinomas (HCCs) in particular, so far none of these candidate biomarkers have been used either for diagnosis or therapy in treating patients. The question remains: Can proteomics identify real biomarkers for HCCs?

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INTRODUCTION

During the past decade, proteomic technologies, including mass spectrometry, have developed considerably, and have been extensively applied to many fields of science, including medicine and pharmacy, as well as industry and agriculture. In the field of medicine in particular, a huge number of reports on the topic have been published. Above all, much effort has gone into proteomic analyses of tissues, cells and sera from cancer patients. The purpose of these studies has been the identification of biomarkers which could provide the development and identification of diagnostic and therapeutic targets for cancers. Many research labs and large pharmaceutical companies have been actively searching for new and effective biomarkers of cancers. Most applications use expression proteomics to determine expression profiles of proteins in tissues, cells and sera during normal or diseased states.

PROTEOMIC BIOMARKERS FOR HEPATOCELLULAR CARCINOMAS

Hepatocellular carcinoma (HCC) is the third most deadly cancer, and about one million patients with HCC die each year. Despite remarkable advances in diagnostic and therapeutic techniques, the incidence of HCC continues to increase. While some papers on the proteomic analysis and discovery of molecular diagnostic markers for the diagnoses against HCC have been reported, no complete molecular diagnostic markers specific to HCC have been revealed by proteomics.
So far, many proteins have been reported as candidates for new diagnostic biomarkers, and as therapeutic targets for HCC by proteomics from HCC tissues. They are classified as (1) digestive enzymes, (2) growth factors, (3) cell adhesion molecules, (4) calcium-binding proteins, (5) proteases, (6) protease inhibitors, (7) transporter proteins, (8) structural molecules, (9) proteins related to cell growth, (10) proteins related to cell differentiation, (11) proteins related to cell transformation, (12) proteins related to tumor invasion, (13) apoptosis inhibitors, (14) proteins related to carcinogen metabolism, (15) molecular chaperone, and (16) others. However, up to now, unfortunately none of them have been able to be used for diagnostic purposes because of their sensitivity and specificity.

**AUTOANTIBODIES AS BIOMARKERS**

Although detection for autoantibodies as diagnostic markers in cancer patients’ sera is useful, not many reports associating them with HCC have been published. Le Naour et al. identified autoantibodies reaction to calreticulin isoforms, cytokeratin 8, cytokeratin 18, creatine kinase B, HSP60, nucleoside diphosphate kinase A and F1-ATP synthase beta-subunit. Takashima et al. identified their reaction to HSP70, peroxiredoxin and Mn-SOD. Their sensitivity seems to be high, but their specificity is still not great enough.

**METABOLOMERIC BIOMARKERS FOR HCCS**

Nowadays, in order to identify dramatically increased or decreased metabolites in cancer tissues, metabolomic profiling analyses have been used. Wu et al. and Xue et al. assayed endogenous metabolome in urine and sera from HCC patients using chemical derivatization followed by gas chromatography/mass spectrometry respectively, and many metabolites were shown to be significantly different between the HCC and control groups.

**CONCLUSION**

To exclude false positive biomarkers for hepatocellular carcinomas (HCCs), we need high specific biomarkers which show as new biomarkers solely in HCCs, and not in hepatitis as well. Many reports have shown such high specific biomarker candidates, unfortunately they are still not enough.

Much time may still be needed for the identification of real biomarkers for HCC.

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