96th Annual Meeting
April 16-20, 2005
Anaheim/Orange County, CA

Abstract Number:	4361
Presentation Title:	Mass spectrometry as a cancer diagnostic tool: a meta-analysis of published data
Presentation Start/End Time:	Tuesday, Apr 19, 2005, 12:10 PM -12:25 PM
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Mass spectrometry is currently the most important proteomic tool. Over the last 3 years, many groups have attempted to use mass spectrometry, in combination with chromatographic techniques and bioinformatics, to diagnose various forms of cancer such as ovarian, prostate, pancreatic, bladder, breast and nasopharyngeal cancer. These methods are based on the premise that the serum proteome and/or peptidome are modified, due to the presence of cancer, in a way that the changes can be captured by mass spectrometric analysis of serum. The diagnostic sensitivities and specificities reported with these methods are far more superior than those obtained using classical cancer biomarkers. However, a review of the literature revealed major discrepancies when the discriminatory peaks between various studies and various cancer types were compared. In most of these studies, the identity of the peaks is unknown. More recent studies have used tandem mass spectrometry to identify discriminatory peaks for ovarian, pancreatic, prostate and nasopharyngeal carcinomas. We examined the abundance of these proteins in serum and their source of origin. The identified proteins include apolipoprotein-A1, transthyretin fragment, inter-alpha-trypsin inhibitor fragment, haptoglobin-alpha-subunit (for ovarian and pancreatic cancer), vitamin D-binding protein (for prostate cancer), serum amyloid A (for nasopharyngeal and pancreatic cancer), alpha-1 antichymotrypsin and alpha-1 antitrypsin (pancreatic cancer). All these proteins are produced by the liver and most of them are acute-phase reactants. The concentration of these analytes in serum are in the range of 1-40 µmol/L, representing high-abundance proteins, in contrast to the classical cancer biomarkers, which are present at sub-nmol/L concentrations.
We conclude that current mass spectrometric analysis of unfractionated serum of cancer patients identifies discriminatory peaks which (a) are present in serum in very high abundance, (b) are produced by the liver and not by cancer cells or their microenvironment. The non-specific nature of these markers (acute-phase reactants) makes it unlikely that these molecules will have high specificity for cancer diagnosis.

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Citation format: Proc Amer Assoc Cancer Res 2005;46:4361.