

STATE-OF-THE-ART LECTURE S2

Tumor-specific serum peptidome patterns

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Recent studies have established distinctive serum peptide patterns through mass spectrometry that correlate with clinically relevant outcomes. Wider acceptance of these ‘signatures’ as valid biomarkers for disease may follow sequence characterization of the components and elucidation of the mechanisms by which they are generated. Using an optimized peptide extraction and MALDI-TOF MS-based approach, we show that a limited subset of serum peptides provides accurate class discrimination between patients with three types of solid tumors (prostate, breast, and bladder) and control individuals without cancer. Sequence analysis of these peptides reveals that they fall into several clusters, and that most are generated by exopeptidase activities that confer ‘cancer-type’-specific differences superimposed on the proteolytic events of the *ex-vivo* coagulation and complement degradation pathways. This small but robust set of surrogate marker peptides provides highly accurate class prediction for an external validation set of prostate cancer samples. As direct MALDI-TOF MS-based serum peptide profiling is in fact activity-based proteomics, i.e., monitoring proteome ‘metabolomic’ products, it is particularly well suited for detection of cancer as proteases are well-established components of cancer progression and invasiveness.