Multiple Myeloma Model Analysis by 21 Tesla FT-ICR Mass Spectrometry

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Multiple Myeloma is a cancer diagnosis with a five-year survival rate below 50%. If the disease is suspected, serum and urine are tested by gel electrophoresis for the presence of elevated levels of a monoclonal antibody (mAb) secreted by bone marrow plasma cells. However, that method can only determine the presence of the malignant plasma cell clones; it cannot determine if the clones have mutated after treatment.
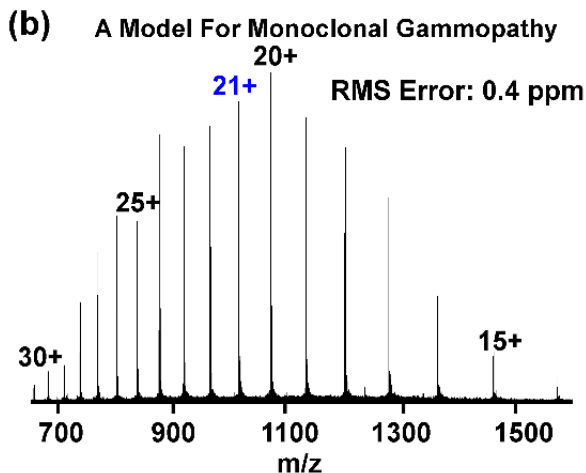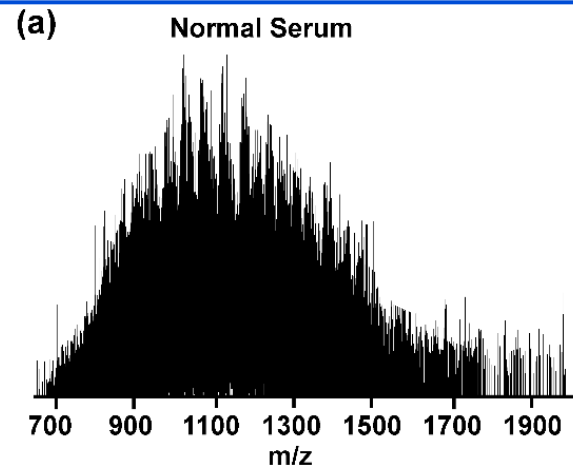
Nano-liquid chromatography 21T Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometry recently analyzed multiple mAb's in serum as a model for multiple myeloma. _This marks the first extensive top-down protein amino acid sequence cleavages for both variable and constant regions for monoclonal antibodies in a human serum background._ The amino acid sequence stratifies samples into different categories corresponding to the DNA sequence, which could one day facilitate personalized cancer diagnosis and a molecular level understanding of multiple myeloma. In addition, detection limits for FT-ICR are ten-fold lower than conventional gel electrophoresis, which should enable earlier diagnosis.

The ultrahigh mass accuracy and extensive residue cleavages from 21T FT-ICR mass spectrometry show great future promise for enhanced-sensitivity diagnosis and monitoring of myeloma cell mutation.

(a) Normal Serum

(b) A Model For Monoclonal Gammopathy
20+ 21+ 25+ 30+ 15+ RMS Error: 0.4 ppm

FT-ICR mass spectra from (a) normal human serum and (b) normal human serum that is spiked with 15 µM of adalimumab as a model for multiple myeloma The data enable the differentiation of adalimumab from other monoclonal antibodies, as well as the identification of the adalimumab light chain isotype.

Facilities: Ion Cyclotron Resonance (21 T FT-ICR MS)