Detection of Minimal Residual Disease in Multiple Myeloma Using RNA Sequencing and Mass Spectrometry

This diagnostic is a method for detecting minimal residual disease in the blood of Multiple Myeloma patients. We have the ability to detect antibodies from the tumor cells at levels approximately 67 times lower than conventional methods, without additional bone marrow biopsies. This exquisite level of detection allows clinicians to better monitor the response to therapies, potentially eliminating minimal residual disease, and perhaps intervene at earlier stages of relapse; all of which enhances the treatment of Multiple Myeloma patients and offers the best chance for a Complete Response.

COMMERCIAL OPPORTUNITY

- Worldwide, 114,000 patients are diagnosed with Multiple Myeloma each year; new agents have greatly increased survival rates (from 12% to 50%) and extended remission periods (up to 7 years); however, patients will typically cycle through multiple treatments, and accurately assessing disease burden to decipher when to terminate therapy is crucial.
- Currently, after a bone marrow biopsy confirms the presence of diseased B cells, patients' serum is monitored weekly during treatment for the antibodies that the tumors secrete; then every 4-12 weeks, as the patient transitions into remission. Unfortunately, the conventional Serum Protein Electrophoresis (SPEP) method is incapable of detecting minimal residual disease (MRD).
- By transforming the RNA sequences from the initial biopsy into peptide signatures that can be assessed using mass spectrometry, our technology offers highly sensitive detection of disease by measuring antibody levels in the serum, through routine blood draws.
- The market for detecting MRD is attractive, as evidenced by Sequenta's Lymphosight™. This technology does so by detecting RNA from tumor cells; however, it requires additional, invasive bone marrow biopsies for monitoring that are painful, costly, and portals for infection in this immune compromised population.

TECHNOLOGY

Pre-clinical studies have shown that utilizing our liquid chromatography-multiple reaction monitoring-mass spectrometry (LC-MRM-MS) method for detecting tumor secreted antibodies in the serum of Multiple Myeloma patients is vastly superior to the serum protein electrophoresis (SPEP) currently employed (MS detects analytes at 0.0015g/dL vs. SPEP at 0.1g/dL). First, we identify the individual tumor cells via RNA based sequencing from the patient's initial biopsy. Next, we translate the RNA encoding the variable chain of the tumor cell's antibody into an amino acid chain. Finally, the chain undergoes multiple rounds of digestion to create peptide fragments that are unique to the tumor signature and appropriate for interrogation by MS. We now know the exact peptide to seek in the serum to inform clinicians of disease burden; moreover, the reaction can be "spiked" with the original peptide sequence that has been heavy labeled to further enhance quantification.

PUBLICATION/PATENT

- ER Remily-Wood et al. (2014) *Proteomics Clinical Appl*ications 8: 783-795
- US provisional patent application filed on 2/28/14 for Dr. Koomen

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