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652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Measuring Minimal Residual Disease in Plasma of Multiple Myeloma Patients By Intact Mass Spectrometry

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Multiple Myeloma (MM) is a hematological cancer that is currently treatable but incurable, and is characterized by the accumulation of malignant plasma cells in bone marrow. Clinical studies have shown that post-cancer treatment, the minimal residual disease (MRD) status is a prognostic factor indicative of the extent of disease remission. MRD assessment has been primarily assessed in bone marrow (BM) using flow cytometry or next generation sequencing. Not only these measurements may lead to false-negative results due to spatial heterogeneity in the BM, hemodilution and/or extramedullary disease as indicated by Derman *et al*. in Blood Cancer Journal ((2021), 11:19) but the procedure for BM collection is invasive and painful for the patient. These authors present a peripheral blood (PB)-based method that potentially can overcome the barriers in assessing for residual disease in MM patients.

We hereby present a non-invasive blood-test for measurement of MRD using mass spectrometry (intact mass approach) for the detection of Ig product in MM patients. We will describe the assay development, analytical characterization of assay performance, and data from the analysis of plasma/serum samples from MM patients enrolled in a clinical trial.

A very low volume of patient plasma/serum sample (10 μL) is required to perform this assay. The plasma/serum sample is diluted in purification buffer, applied to Melon gel resin and incubated for 5 min, followed by centrifugation and reduction with DTT. The supernatant is then analyzed by LC-MS on a Q-Exactive mass spectrometer. Deconvolution of the intact protein m/z spectra is performed to yield intact mass of the specific protein target species of interest.

Overall, the method can process up to 96 samples in parallel within 3 hrs, making this procedure highly scalable for clinical applications.

Data obtained from the assay characterization indicate that the assay is sensitive with an LOD <500 ng/mL and differentiates MM patient from a healthy donor as well allows for the monitoring of MM patient before and after treatment.

In conclusion, although still an exploratory analysis, the blood-based mass spectrometry method can be used to screen for MRD in patients who have undetectable disease by flow cytometry or next generation sequencing.

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