

Researchers use new tool to counter multiple myeloma drug resistance

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Moffitt Cancer Center researchers, and colleagues, are pioneering promising research utilizing a monitoring technology that could provide a better understanding of acquired drug resistance and assist in clinical decision-making for developing individualized patient treatments for multiple myeloma.

"Acquired [drug resistance](#)" (ADR) is a major problem encountered in treating some forms of cancer. The ability to monitor the proteins involved in drug resistance has been a hurdle facing cancer researchers. However, a team of researchers at Moffitt [Cancer Center](#), and colleagues, are pioneering promising research utilizing a [monitoring technology](#) that could provide a better understanding of ADR and assist in clinical decision-making for developing individualized patient treatments for [multiple myeloma](#). The technique has potentially broader applications to other [types of cancer](#) as well.

Their research results are published in the October issue of *Molecular and Cellular Proteomics*.

"Multiple myeloma is an incurable malignancy in the bone marrow," said John M. Koomen, Ph.D., assistant member in Molecular Oncology and [Experimental Therapeutics](#) and scientific director of Moffitt's Proteomics Core Facility. "While patients with multiple myeloma initially respond to chemotherapy, they eventually develop drug resistance from a variety of factors. We want to be able to detect acquired drug resistance, so that we can change the therapeutic regimen

to meet the needs of the patient."

The research team has employed a method called [Liquid Chromatography](#) Multiple Reaction Monitoring (LC-MRM) to monitor proteins determined to be involved in acquired drug resistance. This was based on the prior myeloma research conducted at Moffitt by William S. Dalton, Ph.D., M.D., Moffitt's CEO and center director, and colleagues.

Among the factors in ADR is an alteration in the "apoptotic machinery" of cells. Apoptosis, or programmed [cell death](#), is determined by the interaction of anti-apoptosis and pro-apoptosis proteins in response to both external and internal stimuli. This interaction is known to play a role in ADR.

"Being able to monitor proteins is a major step in understanding multiple myeloma biology and its biomarkers to assist in clinical decision-making and developing personalized cancer therapy," explained Koomen, the study's corresponding author.

LC-MRM has been successfully used to quantify biomarkers of human disease by comparing protein expressions of patients with disease and disease-free controls. LC-MRM has also been used to monitor the signaling pathways and networks in cells. In the method developed by the Moffitt researchers, protein separation techniques are coupled with LC-MRM to quantify selected target proteins.

In their search for apoptosis-regulating signals, the researchers used LC-MRM to quantify the expression levels of proteins in drug-resistant cells vs. non-drug-resistant cells.

Moffitt's "Quantitative Assay Database," or QuAD, used to share methods and reagents for the study of cancer biology, also supported these experiments. QuAD enables the quantitative assessment of the

protein components in cell-signaling pathways and biological processes and holds promise for the systematic investigation of treatment responses in cancer. QuAD is also employed for managing data related to the BRAF gene, which is studied due to its relevance to melanoma, and numerous other genes related to cancer.

"The potential for LC-MRM to assist treatments across diseases is enormous," concluded Koomen. The technology provides new ways to evaluate cancer that can be applied to research and clinical practice.

Provided by H. Lee Moffitt Cancer Center & Research Institute

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