Study Lays Groundwork for Blood Test to Aid in the Detection and Monitoring of Myeloma
Serum MicroRNA Profiles Change as Myeloma Progresses, According to a Report in The Journal of Molecular Diagnostics

Philadelphia, PA, September 30, 2015 – Virtually all patients who develop myeloma have an asymptomatic disease called monoclonal gammopathy of undetermined significance (MGUS) in the years before the onset of myeloma. The five-year relative survival rate for myeloma is 69% for patients diagnosed with stage I or localized disease, compared with 45% for patients with advanced cancer. Nevertheless, only 5% of myeloma cases are stage I when diagnosed. One reason may be the lack of good routine screening tests to identify patients who will progress to myeloma. A new study in The Journal of Molecular Diagnostics found that abnormal levels of microRNAs (miRNAs) detected in the bone marrow of multiple myeloma (MM) patients may also be detectable in peripheral blood, and their measurement may be a way to both mark myeloma onset and track its progression from earlier asymptomatic stages.

Several precursor conditions of myeloma have been recognized, including MGUS and smoldering myeloma (SMM). Although 1% of individuals with MGUS advance to myeloma each year, this rate is 10% for those with SMM. “Currently there is no single factor that can predict patients with MGUS or SMM who are likely to progress to myeloma. A biomarker of disease progression in the peripheral blood could assist in the early identification of patients evolving to multiple myeloma,” explained lead investigator Katherine R. Calvo, MD, PhD, of the Hematology Section of the Department of Laboratory Medicine of the National Institutes of Health (NIH) Clinical Center, Bethesda, MD.

Researchers from the NIH, the National Cancer Institute (NCI), and the Dana-Farber Cancer Institute of Harvard Medical School studied miRNAs as possible biomarkers of myeloma. miRNAs are small non-coding RNA fragments that regulate gene expression and interfere with the production of particular proteins by messenger RNA. Other laboratories have reported increased levels of specific miRNAs in the blood and plasma of myeloma patients. In this study, the investigators analyzed bone marrow, plasma,
and serum samples from healthy controls and patients with myeloma, as well as from patients with MGUS and SMM.

Analysis of fluid from the bone marrow of 20 patients with myeloma resulted in the identification of 111 miRNAs that showed a 2-fold or greater difference from levels observed in eight control samples. Approximately 60% of the miRNAs were down-regulated and 38% were up-regulated. Further analysis revealed a unique miRNA signature indicative of myeloma. The bone-marrow signature included eight members of the let-7 family of miRNAs, each of which showed significant decreases ranging from 6- to 17-fold ($P < .03$) in patients with myeloma.

Other experiments determined the miRNA profiles characteristic of myeloma in peripheral blood serum and plasma samples. Using quantitative real-time PCR to measure the miRNA, 18 miRNAs were found to be significantly decreased in bone marrow myeloma samples; of these, 11 (60%) miRNAs were also significantly decreased in serum samples, and six of the 11 were also found to be lower in plasma samples (including three members of the let-7 miRNA family).

Investigators further explored whether the miRNA pattern of myeloma in precursor diseases changes as the disease progresses. They analyzed serum samples in 17 patients with MGUS, 17 with SMM, 13 with myeloma, and 12 healthy controls. They found that only four of the 11 miRNAs (36%) that were reduced in the myeloma serum samples were lower in the MGUS samples. "This suggests that aberrant expression of these [four] miRNAs may be associated with early events in plasma cell neoplasia," noted Dr. Calvo.

Eight of the 11 (73%) miRNAs were decreased in SMM plasma samples. However, three (27%) were significantly reduced only in the myeloma samples, suggesting that down-regulation of this group of miRNAs may be related to later events during evolution from precursor disease to myeloma.

“Our findings suggest that the antiproliferative and proapoptotic miRNAs, such as the let-7 family members, are down-regulated in multiple myeloma’s microenvironment. These findings suggest that measuring expression of miRNAs associated with myeloma progression in the peripheral blood may hold promise for predicting disease progression in MGUS and SMM," added Dr. Calvo.

Myeloma (also known as multiple myeloma) is characterized by abnormal buildup of plasma cells in the bone marrow and formation of tumors within the bone. In addition to weakening the bone, the tumors prevent the bone marrow from making the healthy blood cells needed to ward off infection and disease. According to the NCI, almost 27,000 individuals will be diagnosed with myeloma in the U.S. in 2015, resulting in 11,240 deaths. Myeloma is the 14th most common cancer and the third most common blood cancer, after lymphoma and leukemia. Men and African-Americans face higher risks of developing the disease.

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NOTES FOR EDITORS

Journalists who would like to request the full text of the study or interview the authors should contact Eileen Leahy at 732-238-3628 or jmdmedia@elsevier.com.

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ABOUT THE JOURNAL OF MOLECULAR DIAGNOSTICS

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