Study lays groundwork for blood test to aid in the detection and monitoring of myeloma

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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