

Myelodysplastic syndromes (MDS) linked to abnormal stem cells

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Researchers at Albert Einstein College of Medicine of Yeshiva University have found that abnormal bone marrow stem cells drive the development of myelodysplastic syndromes (MDS), serious blood diseases that are common among the elderly and that can progress to acute leukemia. The findings could lead to targeted therapies against MDS and prevent MDS-related cancers. The study is published today in the online edition of the journal *Blood*.

"Researchers have suspected that MDS is a 'stem cell disease,' and now we finally have proof," said co-senior author Amit Verma, M.B.B.S., associate professor of medicine and of developmental and molecular biology at Einstein and attending physician in oncology at Montefiore Einstein Center for Cancer Care. "Equally important, we found that even after MDS standard treatment, abnormal stem cells persist in the bone marrow. So, although the patient may be in remission, those stem cells don't die and the disease will inevitably return. Based on our findings, it's clear that we need to wipe out the abnormal stem cells in order to improve cure rates."

MDS are a diverse group of incurable diseases that affect the bone marrow and lead to low numbers of blood cells. While some forms of MDS are mild and easily managed, some 25 to 30 percent of cases develop into an <u>aggressive disease</u> called <u>acute myeloid leukemia</u>. Each year, about 10,000 to 15,000 people in the U.S. are diagnosed with MDS, according to the National <u>Marrow Donor Program</u>.



Most cases of MDS occur in people over age 60, but the disease can affect people of any age and is more common in men than women. Symptoms vary widely, ranging from anemia to infections, fever and bleeding. Treatment usually involves chemotherapy to destroy abnormal blood cells plus supportive care such as blood transfusions.

In the current study, lead author Britta Will, Ph.D., research associate in the department of cell biology, and her colleagues analyzed bone marrow stem cells and progenitor cells (i.e., cells formed by <u>stem cells</u>) from 16 patients with various types of MDS and 17 healthy controls. The stem and progenitor cells were isolated from bone marrow using novel cell-sorting methods developed in the laboratory of co-senior author Ulrich Steidl, M.D., Ph.D., assistant professor of cell biology and of medicine and the Diane and Arthur B. Belfer Faculty Scholar in Cancer Research at Einstein.

Genome-wide analysis revealed widespread genetic and epigenetic alterations in stem and progenitor cells taken from MDS patients, in comparison to cells taken from healthy controls. The abnormalities were more pronounced in patients with types of MDS likely to prove fatal than in patients with lower-risk types.

"Our study offers new hope that MDS can be more effectively treated, with therapies that specifically target genes that are deregulated in early stem and progenitor cells," said Dr. Steidl. "In addition, our findings could help to detect minimal residual disease in patients in remission, allowing for more individualized treatment strategies that permanently eradicate the disease."

More information: The paper is titled, "Stem and progenitor cells in myelodysplastic syndromes show aberrant stage specific expansion and harbor genetic and epigenetic alterations."



Provided by Albert Einstein College of Medicine

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