# Stem cell mobilization therapy found to be safe for bone marrow donors

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According to a study published in *Blood*, the Journal of the American Society of Hematology (ASH), researchers have reported that administration of granulocyte colony-stimulating factor (G-CSF), a drug that releases stem cells from the bone marrow into the blood, is unlikely to put healthy stem cell donors at risk for later development of abnormalities involving loss or gains of chromosomes that have been linked to hematologic disorders such as myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).

G-CSF therapy is given to healthy stem cell donors in order to move the donor's stem cells out of the bone marrow and into the blood stream, a process called mobilization. Once in the blood, large doses of stem cells can be collected safely and without surgery via a process called apheresis, avoiding bone marrow harvest in the operating room. Research has shown that the large doses of mobilized stem cells (called peripheral blood stem cells or PBSCs) can repopulate the bone marrow and create new blood cells faster than stem cells collected directly from the bone marrow, and a number of long-term follow-up studies have demonstrated that healthy donors are not at an increased risk of developing leukemia or other cancers following PBSC donation.

"In recent years, PBSCs have become the dominant source of stem cells for stem cell transplants and the number of transplants performed with PBSCs that have been mobilized with G-CSF has substantially increased. However, the potential for the therapy to cause DNA damage, mutations, or cancer had been suggested in a smaller and less comprehensive prior

study, raising a serious concern within the transplant community and making a definitive study very important. Our study aimed at investigating potential effects of G-CSF on chromosomes in healthy donors," said Betsy Hirsch, PhD, first author of the study and Associate Professor in the Department of Laboratory Medicine and Pathology at the University of Minnesota Medical School.

In order to explore whether G-CSF therapy is indeed a potential cause of chromosome loss or gain in donors, a research team from the University of Minnesota Medical School conducted a study to determine whether there was any risk with short-term, low-dose usage of G-CSF on healthy PBSC donors. The study evaluated blood samples taken from 22 PBSC donors who had received G-CSF and 22 controls with no history of cancer or prior exposure to the therapy over a 12 month period.

Using fluorescence *in situ* hybridization (FISH), a technique that can detect specific targeted regions of DNA in an individual's cells to identify chromosomal abnormalities, the researchers evaluated the white blood cells of the study subjects for aneuploidy, a condition in which there is an abnormal number of chromosomes. Loss and gain of chromosomes represent one form of chromosome instability that is frequently a step in the development of cancer. Specifically, the researchers focused on chromosome 7 and a series of other chromosomal regions well documented to be associated with MDS and AML. The researchers also evaluated the cells to determine if both copies of a given chromosome replicated in synchrony or asynchronously, as asynchronous replication can also signal genomic instability and a higher risk of chromosomal abnormalities.

"Contrary to the previously published data, our study concludes that G-CSF stimulation does not result in replication asynchrony or induce the atypical levels of abnormality for chromosome 7 or other chromosomes that have been associated with MDS and AML, and we expect that these

results can be generalized to all chromosomes," said Dr. Hirsch.

Jeffrey McCullough, MD, senior study author and Professor in the Department of Laboratory Medicine and Pathology at the University of Minnesota Medical School, added, "Furthermore, our data support the conclusion that G-CSF does not induce chromosomal instability through the PBSC mobilization process and remains a safe therapy for healthy stem cell donors."

Provided by American Society of Hematology