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Researchers discover mechanism controlling the development of myelodysplastic

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Researchers at the Moffitt Cancer Center have discovered a control mechanism that can trigger the development of myelodysplastic syndromes (MDS), a group of blood cancers. This finding may lead to therapies capable of preventing the progression of these diseases.

MDS primarily affects older individuals, with approximately 12,000 new cases diagnosed each year. In MDS, a person's blood is not able to make one or more types of healthy blood cells—red blood cells, white blood cells or platelets. Instead, the patient has a high number of immature stem cells that do not develop properly. This can lead to anemia and a higher risk of infection and bleeding. MDS patients also have an increased risk of developing leukemia. Unfortunately, there is no effective therapy for MDS and scientists do not have a clear answer on how MDS develops.

In their translational study, Moffitt clinical and basic science researchers found that MDS patients have a higher number of suppressor cells in their bone marrow. These suppressor cells promote inflammation and prevent blood stem cells from developing properly. Inflammation is known to be involved in the development of different types of cancer.

"We discovered that two different molecules, S100A9 and CD33, in the myeloid-derived suppressor cells bound to one another to promote inflammation leading to the development of MDS," said Sheng Wei, M.D., associate member of Moffitt's Immunology Program.

These researchers created a mouse model of human MDS based on their discovery. They used the model to show that by targeting the myeloid-derived suppressor cells and blocking the CD33 molecule's ability to communicate, blood cells were able to develop normally.

"Our findings suggests small molecular drugs targeting the S100A9 and CD33 molecule's signaling pathways can be developed to make myeloid-derived suppressor cells inactive," noted Wei. "Now we are collaborating with a pharmaceutical company to develop a phase I trial targeting this pathway on humanized monoclonal antibodies, which are mice antibodies that have been modified to be similar to human antibodies."

The researcher added that the results from this study may have an impact on more than just MDS patients because higher levels of myeloid-derived suppressor cells are found with several other types of cancer.

The study appeared in the Nov. issue of the *Journal of Clinical Investigation*.

Provided by H. Lee Moffitt Cancer Center & Research Institute