Researchers find novel predictor for MDS progression risk

September 13 2012

Researchers at Moffitt Cancer Center and colleagues have discovered that changes in the physical characteristics of the effector memory regulatory T cell can predict the progression risk of myelodysplastic syndromes (MDS) to acute myeloid leukemia. The finding could improve prognostication for patients with MDS and better inform therapeutic decision making.

The study published in the August issue of The *Journal of Immunology*.

Awareness of the condition increased earlier this year when ABC's "Good Morning America" co-anchor Robin Roberts announced that she is battling MDS. Formerly known as pre-leukemia, MDS is a collection of blood disorders. One in three patients with MDS develops bone marrow failure and progresses to acute myelogenous leukemia within the first few years after diagnosis.

MDS involves the ineffective production of blood cells in bone marrow and often leaves patients anemic and in need of frequent blood transfusions.

The disease may develop as the result of chemotherapy or radiation for cancer treatment or can be related to bone marrow failure resulting from frequent transfusions and subsequent iron overload. Because the body has no natural means to reduce iron that accumulates from repeated transfusions, a patient's organs can become overloaded with iron, leading to heart failure, liver injury, susceptibility to infection and other

complications. Bone marrow transplantation may be necessary.

Seeking to understand more about the development of MDS, Moffitt researchers and their colleagues investigated aspects of the immune system, particularly the role of regulatory T cells, also known as Tregs. Tregs, said the researchers, are well-defined players in tumor immune invasion in solid tumors, but little is known about the role Tregs play in pre-malignant human diseases.

"We investigated a Treg subset called 'effector memory Tregs,' " said study senior author Pearlie K. Epling-Burnette, Pharm.D., Ph.D., senior member of Moffitt's Immunology Department. "We found that changes in the physical characteristics, or phenotypes, of Tregs in MDS suggest that they may be recently activated in a manner similar to effector memory T cells. By looking at a patient's effector memory Treg cells, we were able to identify patients at higher risk for MDS progression."

An increase in effector memory Tregs likely reflects active immune suppression and may represent the earliest biomarker indicating conversion to an immunosuppressive microenvironment, the researchers said.

The team concluded that the changes to effector memory Treg phenotype may also be a useful tool for identifying MDS patients who may respond to specific classes of drugs. This would make inclusion of a patient's Treg status into prognostic and treatment models potentially valuable for informing therapy decisions for patients with MDS.

"Our study sheds light on a unique aspect of T cells and immunity in a pre-malignant model of disease and specifically implicates the importance of changes to effector memory Tregs," concluded Epling-Burnette and her co-authors. "Our findings specifically implicate effector Treg expansion in disease progression in MDS."

Provided by H. Lee Moffitt Cancer Center & Research Institute