HUTCH NEWS

Markers for measuring MDS

Gene AF1q may help researchers better understand, classify and treat collection of different disorders known as myelodysplastic syndrome

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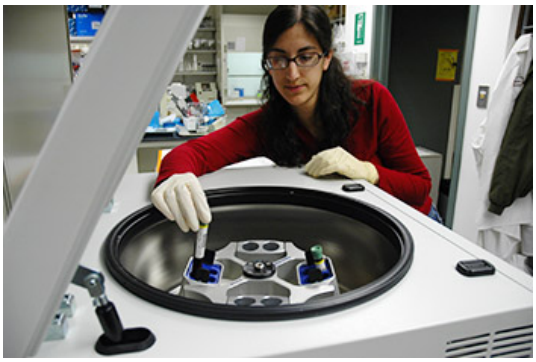

Nissa Abbasi, research assistant, works in the Deeg lab. A discovery by researchers in the lab may improve outcomes for patients with MDS.
Photo by Todd McNaught

Myelodysplastic syndrome (MDS) is a puzzling, life-threatening set of disorders for which there are no easy cures or quick remedies. Symptoms can range from weakness and excessive bruising to debilitating fatigue, and MDS may progress to leukemia. The variable nature of MDS has made it hard to develop a reliable system to classify the disease, which makes it challenging for doctors to predict prognosis and, therefore, choose appropriate treatment.

A new approach led by Dr. Joachim Deeg and his colleagues in the Clinical Research Division offers promise for improving the ability to classify the disease, which ultimately could improve patient care and outcomes. The researchers recently discovered that the increased expression of a gene called AF1q may correlate with an MDS patient's prognosis. Their report appeared in the January issue of the British Journal of Haematology.

In the study of 47 patients with MDS, a progressive increase in the expression of AF1q was associated with progression of MDS to more advanced stages. "Patients who have an early stage or a less aggressive presentation of MDS tend to have low levels, and patients with more advanced disease have significantly higher levels," Deeg said.

Current classification system

"Part of the difficulty of treating MDS results from the broad spectrum of disorders listed under the same heading and the lack of clinical and molecular markers to classify and stage the different forms," Deeg said. He and others hope to identify new markers that may help to determine a patient's prognosis. The current MDS classification system, known as the International Prognostic Scoring System (IPSS), grades the severity of the patient's MDS in terms of shortened life expectancy and the chance of transformation of the disease to acute myeloid leukemia (AML), a type of blood cancer. While the IPSS has enhanced prognostic accuracy in comparison to older classification schemes, every MDS patient has a different set of symptoms.

"Anyone working with MDS right now agrees that the classification system we have is not satisfactory. It's very crude," Deeg said. "More importantly, what we currently call MDS is really a collective term for a number of different diseases. We call them MDS for lack of a better term, but as we develop an improved understanding — and maybe genes such as AF1q are going to help us — we will classify and treat these diseases differently."

The researchers, led by Dr. William Tse (formerly a Fred Hutchinson researcher and now at Case Western University), also found that increased expression of the AF1q gene correlated with a decreased ability for cells to undergo cell death — a feature common among cancers that progress and become harder to treat. Another paper on this gene marker published by Tse and colleagues last year showed that children with acute leukemia, with high levels of expression had a worse prognosis than patients with low levels.

Deeg is hopeful that improved understanding of the molecular biology of MDS will eventually also improve treatment. "It may well be that the findings with AF1q, along with techniques such as gene-expression arrays, flow cytometric analysis and functional studies, will refine the classification of what we currently call MDS," he said. "It might help with prognosis and treatment."

MDS is an umbrella term for a collection of disorders in which the bone marrow does not produce enough mature blood cells. Normally, the bone marrow produces three major types of blood cells: red blood cells (which carry oxygen to the blood), white blood cells (which help the body fight infections) and platelets (which help the blood clot). For MDS patients, this process breaks down. Blood cells do not develop properly, and as a result, there is a lack of healthy blood cells in the body.

An estimated 15,000 to 20,000 new cases of MDS are diagnosed in the United States each year. The average age at the time of diagnosis is about 70 years. MDS is often not considered a cancer, although it has all the characteristics of a malignancy. Formerly known as preleukemia, MDS progresses to AML in some patients.

The average survival period for MDS patients varies from a few months to five to 10 years. Presently, the only cure for severe MDS is a stem-cell transplant; however, since more than half of all affected people are over age 70, the procedure may not be well tolerated. More recently developed strategies for transplantation, which use reduced intensity, non-myeloablative conditioning regimens (also called "mini-transplants"), show some promise in treating MDS in older patients.

Relapse risk

Deeg and his colleagues, Drs. Jerald Radich and Derek Stirewalt, are continuing to analyze gene-expression patterns in MDS, which may lead to potential targets for gene therapy. Deeg also hopes to determine whether high levels of AF1q expression indicate a high risk of relapsing after transplantation, which might lead to different approaches in the preparation of patients for transplantation.

Co-authors included Drs. Stirewalt, Radich, Fred Appelbaum and Theodore Gooley, all of Fred Hutchinson.

TAGS: Clinical Research, H Joachim Deeg, Myelodysplastic Syndrome

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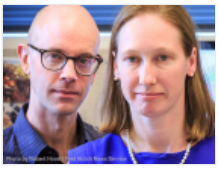

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