NOVEL PROGNOSTIC SNP IN CN-AML

Recent work has identified a single nucleotide polymorphism (SNP) as a novel prognostic marker in cytogenetically normal acute myeloid leukemia (CN-AML). Frederik Damm and colleagues located this SNP in the mutational hotspot of Wilms tumor 1 (*WT1)* in individuals with CN-AML and found it to be an independent predictor of a favorable outcome in these patients. "*WT1* has been an interesting gene in hematology for almost 20 years, and we wanted to conduct a combined analysis on *WT1* expression and mutations," comments Damm.

The researchers sequenced exon 7 and exon 9 of *WT1* in 249 patients with CN-AML and 50 healthy controls, and analyzed the data for associations between mutations in the *WT1* sequence and disease outcome. Damm's team found the minor allele of the SNP—termed rs16754 ($WT1^{AG/GG}$)—in 25.7% of patients with CN-AML and 36% of healthy participants. Overall, although SNP rs16754 was not associated with disease susceptibility, it was favorably prognostic in individuals with CN-AML, and predicted relapse-free survival (hazard ratio (HR) 0.49, 95% CI 0.3–0.81, $P=0.005$) and overall survival (HR 0.44, 95% CI 0.27–0.74, $P=0.002$). By contrast, no other molecular marker (including *NPM1* or *CEBPA*) could identify a favorable prognosis in these patients.

Interestingly, the prognostic strength of SNP rs16754 was elevated in patients classified as high-risk on the basis of *NPM1*/*FLT3*-internal tandem duplications, a finding that might have important clinical utility. "As high-risk patients normally undergo bone marrow transplantation, with the risk of transplant-related mortality, it is of clinical importance to identify patients who are likely to benefit from a bone marrow transplantation," concludes Damm, who predicts that "our study might help to address this issue".

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Original article Damm, F. *et al*. Single nucleotide polymorphism in the mutational hotspot of *WT1* predicts a favorable outcome in patients with cytogenetically normal acute myeloid leukemia. *J. Clin. Oncol.* **28**, 578–585 (2010)