Leukemia cells from 64 adults (<60 years old) who had high-risk molecular features of AML (*FLT3*-ITD, wild-type *NPM1*, or both) were profiled for microRNA expression. The investigators found 12 microRNA probes that were associated with event-free survival ($P<0.005$). Increased expression of five of these probes (corresponding to members of the microRNA-181 family) was associated with decreased risk of a future event. Increased expression of the remaining seven probes was positively related to future risk. In multivariable analysis, the association between microRNA expression summary value and outcome was independent of white-cell count and the *FLT3*-ITD:wild-type *NPM1* ratio ($P=0.04$ and $P=0.02$, respectively). In addition, increased microRNA summary values were associated with the increased expression of genes involved in innate immunity in AML. Expression levels of 32 of these genes, including those that encode interleukin 1β and members of the Toll-like receptor family, were found to be inversely related to expression levels of microRNA-181 family members.

The authors suggest that downregulation of the microRNA-181 family contributes to the development of AML through the activation of pathways controlled by Toll-like receptors and interleukin 1β.

Original article Marcucci G *et al.* (2008) MicroRNA expression in cytogenetically normal acute myeloid leukemia. *N Eng J Med* **358:** 1919–1928

Mutations in patients with cytogenetically normal AML predict treatment outcome

Patients with cytogenetically normal acute myeloid leukemia (AML) represent around 40–50% of all AML cases and are categorized as an intermediate-risk group. This group of patients is heterogeneous, with mutations occurring in several genes involved in different processes related to leukemogenesis, which can affect prognosis. Schlenk and colleagues, therefore, investigated the prognostic and predictive value of mutations in the following genes in patients with cytogenetically normal AML: nucleophosmin (*NPM1*); fms-related tyrosine kinase 3 (*FLT3*); CCAAT/enhancer binding protein α (*CEBPA*); myeloid–lymphoid or mixed-lineage leukemia (*MLL*); and the neuroblastoma RAS viral oncogene homolog (*NRAS*).

A total of 872 patients with newly diagnosed AML (aged 16–60 years) who were enrolled in four separate German–Austrian Acute Myeloid Leukemia Study Group trials were assessed. In all four trials, allogeneic stem-cell transplantation was recommended in patients with a related donor matched for human leukocyte antigen. Mutant *NPM1*, without *FLT3*-internal tandem duplication (ITD), and mutant *CEBPA* were significantly associated with complete remission after induction chemotherapy and were associated with a significantly better relapse-free and overall survival. Only patients with the genotypes *FLT3*-ITD or wild-type *NPM1*/*CEBPA* without *FLT3*-ITD benefited from allogeneic stem-cell transplantation; stem cell transplantation did not confer a survival benefit on patients with more-favorable genotypes.

The authors recommend that newly diagnosed patients with AML should be screened for *NPM1, FLT3*, and *CEBPA* mutations, as the data from such analyses provide important prognostic information and may influence the choice of post-remission therapy.

Original article Schlenk RF *et al.* (2008) Mutations and treatment outcome in cytogenetically normal acute myeloid leukemia. *N Engl J Med* **358:** 1909–1918