Mutant *NPM1* predicts outcome in younger adults with AML and normal cytogenetics

Around 50% of patients with acute myeloid leukemia (AML) do not show chromosomal aberrations on conventional analysis. A study has shown that *NPM1* mutations in the absence of *FLT3* internal tandem duplications (ITDs) define a distinct molecular and prognostic subclass of young adult AML patients with normal cytogenetics.

The nucleophosmin (*NPM1*) gene is known to be involved in a number of chromosome translocations associated with leukemia and lymphoma, and mutations in this gene are the most frequent events identified in adult AML with normal karyotype. This trial examined the incidence and prognostic relevance of *NPM1* mutations in a series of 300 homogenously treated adults (16–60 years old) with AML and normal cytogenetics. Treatment regimens included double-induction therapy and consolidation therapy with high cumulative doses of cytarabine. Mutations in *NPM1* were seen in 48% of patients and were associated with specific clinical, phenotypic and genetic features. The potential association of these mutations with *FLT3* and *CEBPA* mutations was also examined, showing a significant interaction of *NPM1* and *FLT3* ITDs. The presence of *NPM1* mutations predicted better response to induction therapy and multivariate analysis showed that *NPM1*-mutated/*FLT3* ITD-negative status and mutated *CEBPA* were predictive of favorable overall survival ($P<0.0001$ and $P=0.05$, respectively).

Comprehensive molecular screening can allow for the classification of subclasses within young adult AML patients. It could lead to improved risk stratification and better treatment outcome, while minimizing toxicity.

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Original article Döhner K *et al.* (2005) Mutant *nucleophosmin (NPM1)* predicts favorable prognosis in younger adults with acute myeloid leukemia and normal cytogenetics—interaction with other gene mutations. *Blood* [doi: 10.1182/blood-2005-05-2164]

Hyaluronan levels and endometrial cancer progression

There is increasing evidence for the role of the extracellular glycosaminoglycan hyaluronan (HA) and its degradative enzymes hyaluronidases (Hyal) in tumor progression. HA is thought to facilitate tumor metastasis by promoting tumor-cell adhesion and migration. Hyal might enhance tumor invasion by facilitating extracellular matrix degradation and tumor angiogenesis. Elevated levels of HA and Hyal have been found in a range of tumors, including those of the prostate, breast and bladder.

This study analyzed the expression and cellular localization of HA and its synthase enzymes, together with the mRNA expression of Hyal, in 39 samples of endometrial cancer of varying histological grade. HA, its synthases and degradative enzymes were identified in all endometrial cancers. Histochemical analysis showed that HA was predominantly localized to tumor stroma. Levels increased with tumor grade, although this was significant only in Grade 2 carcinomas. HA staining intensity correlated with extent of myometrial invasion. HA synthase was localized mainly to tumor epithelial cells, and levels did not vary with tumor grade. Real-time reverse transcription polymerase chain reaction showed Hyal 3 to be the most abundant isozyme, followed by Hyal 2, with Hyal 1 the least abundant. There was no variation with tumor grade in the mRNA levels of any of the Hyal isozymes.

Although further studies are needed to fully understand the role of HA in tumorigenesis, these results suggest that elevated HA has a possible role in endometrial cancer progression and could offer potential as a prognostic marker.

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Original article Paiva P *et al.* (2005) Expression patterns of hyaluronan, hyaluronan synthases and hyaluronidases indicate a role for hyaluronan in the progression of endometrial cancer. *Gynecol Oncol* **98:** 193–202

AMN107: a potential therapy in myeloproliferative disease

The small molecule tyrosine kinase inhibitor AMN107 was initially designed as a potent novel BCR-ABL inhibitor, and shows activity against a number of *BCR-ABL* mutations known to confer resistance against imatinib. It is currently undergoing phase II clinical trials in patients with *BCR-ABL*-positive chronic myeloid leukemia and acute