GLOSSARY

EGFR
Epidermal growth factor receptor; inhibited by both gefitinib and 4,5-dianilinophthalimide

ERBB2
An epidermal growth factor receptor-related receptor tyrosine kinase that is inhibited by both gefitinib and 4,5-dianilinophthalimide

Treatment of acute myeloid leukemia with gefitinib: clinical trials recommended

Investigators have identified an FDA-approved drug that increases the degree of myeloid maturation in patients with mutations in differentiation-promoting transcription factors. They advocate gefitinib (Iressa®, AstraZeneca UK Limited, London, UK) as a promising alternative to cytotoxic agents for treating acute myeloid leukemia (AML).

Stegmaier *et al*. found neutrophilic and myeloid differentiation in AML cell lines (HL-60 and Kasumi-1) that had been treated with 10 μM gefitinib for 4 days. After 6 and 24 hours of 10μM gefitinib treatment, the two cell lines demonstrated significant genome-wide gene expression of neutrophil maturation. This was also evident in the AML cell blasts obtained from eight patients. Consistent with the excellent clinical safety profile of gefitinib, the researchers found that cell viability was reduced in AML blasts but not in normal donor blood cells. Previous assumptions that EGFR or ERBB2 inhibition is involved in the mechanism behind differentiation were proved false as EGFR and ERBB2 transcripts were undetectable in HL-60 and Kasumi-1 cell lines.

Gefitinib binds to a large number of different kinases and the mechanism might involve inhibition of one or a combination of these. Further study into the drug's functioning, and immediate commencement of clinical trials are essential if we are to make use of this exciting development.

Rachael Williams

Original article Stegmaier K *et al.* (2005) Gefitinib (Iressa) induces myeloid differentiation of acute myeloid leukemia. *Blood* **106:** 2841–2848

NAT2 and *GSTM1* polymorphisms affect the risk of bladder cancer

A study recently published in *The Lancet* has revealed strong associations between two carcinogen-detoxifying genes—*NAT2* and *GSTM1*—and the risk of bladder cancer. The research by García-Closas and co-workers investigated polymorphisms in several *NAT* and *GST* genes in participants in the Spanish Bladder Cancer Study.

DNA samples were provided by patients ($n = 1{,}150$) diagnosed with carcinoma of the urinary bladder, and control individuals ($n = 1{,}149$) matched for age, sex, and geographical region who had been admitted to participating hospitals for unrelated conditions. All patients were white and were predominantly male.

The risk of bladder cancer was 40% higher in patients with *NAT2* slow-acetylator genotypes than in intermediate-acetylator or rapid-acetylator genotypes ($P = 0.0002$). Regression analysis also revealed a stronger association between smoking and risk of bladder cancer among *NAT2* slow-acetylator genotypes, than among either intermediate-acetylator or rapid-acetylator genotypes ($P = 0.008$). Individuals with the *GSTM1* null genotype also had a significantly increased risk of bladder cancer compared with those who had one or two copies of the gene ($P < 0.0001$), although the relative risk was not affected by smoking status. No significant interactions were found for the other genetic polymorphisms investigated. The authors also used the data from this study to update several previously published meta-analyses, which supported the convincing associations between bladder cancer and both *NAT2* slow-acetylation and *GSTM1* deletion.

Alexandra King

Original article García-Closas M *et al.* (2005) *NAT2* slow acetylation, *GSTM1* null genotype, and risk of bladder cancer: results from the Spanish Bladder Cancer Study and meta-analyses. *Lancet* **366:** 649–659

Effective salvage therapy for children with recurrent extragonadal germ-cell tumors

Data on the therapeutic options for children with recurrent extragonadal germ-cell tumors (GCTs) are scarce. In response to this situation an international research group has presented a review of high-dose chemotherapy (HDC) and hematopoietic-progenitor-cell support salvage therapy in these patients, a strategy until now investigated primarily in adults.

Pediatric patients ($n = 23$) with a diagnosis of relapsed extragonadal GCT, who had undergone HDC salvage therapy, were selected from the European Group for Blood and Bone Marrow Transplantation register. Data

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