Distinct mutations of *FLT3* result in different outcomes in patients with AML

In patients with acute myeloid leukemia (AML), internal tandem duplications (ITDs) within the tyrosine kinase protein FLT3 correlate with increased relapse rates and poor overall survival (OS); however, the prognostic impact of mutations in the tyrosine kinase domain (TKD) of FLT3 is currently unknown.

In a recent study, 1,107 young adults with AML of known *FLT3*-ITD mutation status were screened for *FLT3*-TDK mutations. Overall, *FLT3*-TDK mutations were identified in 127 patients, and their presence was associated with an increased white blood cell count ($P = 0.006$). Patients with inv(16) chromosomal translocation were significantly more likely to harbor *FLT3*-TDK mutations than were patients without this translocation ($P = 0.005$). By contrast, *FLT3*-TDK mutations were rare in subjects with adverse cytogenetics ($P = 0.008$) and in patients with secondary AML. The 5-year OS rate was higher in patients with *FLT3*-TDK mutations than in TKD-mutation-negative patients (53% and 37%, respectively; $P = 0.002$). Comparison of *FLT3*-TDK versus *FLT3*-ITD mutation carriers showed statistically significant differences in OS (odds ratio 0.53; $P < 0.001$) and cumulative incidence of relapse (odds ratio 0.45; $P < 0.001$). In multivariate analysis, patients with a high proportion of mutated *FLT3* alleles (i.e. greater than the median level of 25%) had a higher rate of OS at 10 years than did wild-type patients or patients who had a low relative *FLT3* mutation level ($P = 0.004$).

The authors suggest that distinct mutations of *FLT3* correlate with different clinical outcomes and that this finding might have implications for the management of patients with AML.

Original article Mead AJ *et al.* (2007) FLT3 tyrosine kinase domain mutations are biologically distinct from and have a significantly more favorable prognosis than FLT3 internal tandem duplications in patients with acute myeloid leukemia. *Blood* **110:** 1262–1270

Low-dose radiation induces apoptotic and immunological responses in patients with FL

Low-dose involved-field radiotherapy is an effective palliative therapy for patients with follicular lymphoma (FL); however, the molecular mechanisms underlying the response to radiation remain unknown. A study by Knoops *et al.* used gene-expression analysis to examine the molecular mechanisms involved in radiation sensitivity.

The authors compared the gene-expression profiles of 15 excisional or large-needle biopsy samples removed from patients with FL before and after irradiation. Most of the genes induced by low-dose radiation were identified as being related to at least one of three processes: the p53 pathway; the immune response; or cell-cycle regulation. A Gene Ontology analysis revealed significant over-representations of cell-cycle and immune response genes in the gene set induced by low-dose radiation ($P = 0.001$ for both). Irradiation also induced the expression of 25 p53-regulated targets. Immunohistochemical analysis confirmed these results, showing an increase in p53-positive cells from 5% before radiation to more than 80% after radiation, as well as demonstrating activation of the intrinsic and extrinsic p53-induced cell death apoptotic pathways. Genes related to the activation of macrophage or dendritic cells, and T-helper-1-related immune responses were also upregulated following irradiation. Immunohistochemical analysis for CD68 and p53 suggested that macrophages might be activated specifically by apoptotic cells to induce apoptotic body clearance.

This is the first *in vivo* report of an immunologically active, p53 apoptotic response in patients receiving low-dose radiation therapy for FL. Moreover, these results support the use of low-dose radiotherapy as a palliative treatment for patients with FL.

Original article Knoops L *et al.* (2007) In vivo p53 response and immune reaction underlie highly effective low-dose radiotherapy in follicular lymphoma. *Blood* **110:** 1116–1122

Duplicated *TMPRSS2–ERG* fusion predicts extremely poor outcome in prostate cancer

The recently reported association between fusion of the *TMPRSS2* and *ERG* genes and prostate cancer has raised the possibility that alterations at the *ERG* locus could provide prognostic information independent of that provided by Gleason score. Now, Attard *et al.* have assessed the prognostic utility of *ERG* locus alterations in a cohort of 445 conservatively managed patients with prostate cancer.