GLOSSARY

P-GP
P-glycoprotein

BCRP
Breast cancer resistance protein

MRP1 AND MRP2
Multidrug-resistance-associated proteins 1 and 2

Genetic basis of drug resistance in childhood ALL

Current drug treatments fail in about 20% of children with acute lymphoblastic leukemia (ALL). Holleman and colleagues have investigated the multiple pathways governing drug resistance in their recent gene-expression profiling study.

Leukemia cells from 173 children were first tested for sensitivity *in vitro* to the drugs prednisolone, vincristine, asparaginase and daunorubicin. Genes that were differentially expressed in drug-resistant and drug-sensitive cells were then identified by means of an oligonucleotide microarray. Finally, gene-expression signatures associated with resistance or sensitivity to each of the four drugs were compared with treatment outcome in both the original cohort and a second cohort of 98 children.

A total of 124 genes, belonging to numerous functional groups, were differentially expressed in cells resistant or sensitive to prednisolone (33 genes), vincristine (40 genes), asparaginase (35 genes) or daunorubicin (20 genes). Of these genes, 121 had not previously been linked to resistance to these drugs. Multivariate analysis indicated that expression of genes associated with drug resistance had an independent influence on outcome of treatment in both the original 173 patients and the validation cohort, who were being treated at a different center.

Holleman *et al.* conclude that differential expression of relatively few genes is linked with treatment response in childhood ALL, and that these genes may provide targets for improved therapy.

Original article Holleman A *et al.* (2004) Gene-expression patterns in drug resistant acute lymphoblastic leukemia cells and response to treatment. *New Engl J Med* **351:** 533–542

Health-related quality of life in breast cancer

Health-related quality of life (HRQOL) is a good prognostic indicator in breast cancer but has only recently been included as an outcomes measure in clinical trials. To investigate HRQOL and its associated factors in women treated for early stage breast cancer within the previous 4 years, Bardwell *et al*. have analyzed a subset of data from the Women's Healthy Eating and Living (WHEL) Study.

Women ($n = 2582$) completed the RAND-36 Health Survey, which includes four mental and four physical subscales measured from 0–100. Comparisons were made with US population norms and results from other breast cancer studies.

HRQOL was generally similar to population norms. Clinically meaningful differences were seen, however, in the 'role limitations—due to physical problems' subscale (6.7 points worse for the study population than for norms) and for 'social functioning' (5.2 points better for the study population than for norms). Comparisons with two other breast cancer studies again showed similar HRQOL, except for 'role limitations—due to emotional problems', in which the WHEL study participants were 5.1 points healthier. Multivariate analysis revealed that better physical HRQOL was linked to fewer psychological symptoms, lower body mass index, better sleep quality and more physical activity ($P \leq 0.001$). Better mental HRQOL was related to better sleep quality, fewer life events, less pain and fewer gastrointestinal symptoms.

The study demonstrates that HRQOL was influenced by several factors. Bardwell *et al.* suggest that clinical interventions targeting some of these variables may improve HRQOL in these patients.

Original article Bardwell WA *et al.* (2004) Health-related quality of life in women previously treated for early-stage breast cancer. *Psycho-Oncology* **13:** 595–604

The blood–testis barrier in health and disease

Chemoresistance of metastatic testicular tumors is thought to be mediated partly by the blood–testis barrier (BTB), which impedes delivery to the testis of certain cytotoxic agents. Little is known, however, about the arrangement of drug-efflux pumps within this barrier. Bart *et al.* have studied the localization of the efflux pumps P-GP, BCRP, MRP1 and MRP2 to better understand the role of the BTB.

Immunohistochemical staining for the four efflux pumps was performed on normal testicular tissue ($n = 12$), non-pretreated nonseminoma ($n = 10$), seminoma ($n = 10$) and testicular lymphoma ($n = 9$) and expression was assessed semiquantitatively. Newly formed blood vessels were localized using factor VIII staining.