PancPRO is based on the framework developed for BRCAPRO, a well-documented risk predictor in breast cancer. The PancPRO model uses family history to estimate the probability of an individual harboring a susceptibility gene, and of subsequently developing pancreatic cancer. The model was validated in 6,134 individuals from 961 families; 26 individuals were diagnosed with incident pancreatic cancer a mean of 2.3 years after enrollment. The number of observed cases of pancreatic cancer was not significantly different from the number of expected cases (26 vs 31), and the model showed good discriminatory ability (area under the receiver operating characteristic curve of 0.75).

The authors present PancPRO as the first risk prediction tool for pancreatic cancer, allowing assessment of genetic risk without knowledge of causative genes. The model is freely available as part of the BayesMendel package from http://www.cancerbiostats.onc.jhmi.edu/BayesMendel. The authors hope that the model will help to identify at-risk individuals suitable for inclusion in trials of early detection programs.

Original article Wang W *et al.* (2007) PancPRO: risk assessment for individuals with a family history of pancreatic cancer. *J Clin Oncol* **25:** 1417–1422

Genomic analysis detects two distinct molecular subtypes of ER-positive breast cancer

Distinct molecular subtypes of breast cancer, defined through microarray analysis, have been shown to have different clinical outcomes. Basal and ErbB2-type breast cancers are frequently recognized, but distinguishing the estrogen receptor (ER)-positive subtypes is problematic, not least because no simple diagnostic test exists. Loi *et al.* used their previously developed gene-expression grade index (GGI) to identify two distinct molecular subtypes of ER-positive breast cancer. The index works by averaging the expression level of a gene set (up to 97 genes) in order to determine the concordance between a tumor sample and histological grade.

ER-positive breast cancers were categorized as being of high or low genomic grade by use of the GGI, and classifications were compared with those made by existing molecular tools. The two ER-positive molecular subtypes identified by the GGI had similar biological pathways, but correlated closely with the luminal A and B subtypes by hierarchical cluster analysis, and showed strong agreement with the risk subgroups produced by the 21-gene recurrence score. High genomic grade was associated with a worse clinical outcome than was low genomic grade in patients treated with adjuvant tamoxifen only, as well as in those who were untreated. The GGI was a stronger prognostic variable than traditional clinical prognostic factors in univariate and multivariate analyses.

The authors conclude that the GGI is simple to use and gives highly reproducible results across multiple data sets. They note that these data reinforce the role of cell-cycle and grade-related genes in determining prognosis in patients with ER-positive breast cancers.

Original article Loi S *et al.* (2007) Definition of clinically distinct molecular subtypes in estrogen receptor-positive breast carcinomas through genomic grade. *J Clin Oncol* **25:** 1239–1246

The radiation sensitizer AK-2123 prolongs survival in patients with stage III cervical cancer

Patients with locally advanced cervical cancer have a poor prognosis because radiotherapy fails to control local disease. The low efficacy of radiotherapy in the treatment of local disease is attributed to the presence of a less radiosensitive hypoxic cell population. Studies of AK-2123, a nitrotriazole hypoxic cell sensitizer, have shown encouraging results in patients with uterine and head and neck cancers. A recent phase III randomized trial has evaluated AK-2123 in combination with radiotherapy in the treatment of advanced cervical cancer.

The study included 326 patients with stage IIIA or IIIB squamous cell carcinoma of the uterine cervix. Participants were randomized to receive either standard radical radiotherapy (RT) alone, or radiotherapy and AK-2123 (RT+AK-2123). Patients treated with RT+AK-2123 had a significantly higher initial rate of complete response than patients treated with RT alone (65% and 52%, respectively; $P=0.01$), and this difference was also observed in subgroup analysis. The rate of local tumor control was 61% after RT+AK-2123 and 46% after RT alone ($P=0.005$). At 60 months, actuarial survival rates were 57% and 41% for patients treated with RT+AK-2123 and RT, respectively (logrank $P=0.01$). AK-2123 was generally well