GLOSSARY

ACRAL
Classified as being from the non-hair-bearing skin of soles of the feet, palms, or under the nails

SEER PROGRAM
A program run by the National Cancer Institute of the National Institutes of Health that periodically reports estimates of cancer incidence and mortality in the US

Genetic alterations in melanoma explain differing reactions to UV light

Exposure to ultraviolet (UV) light is a major factor in the rising incidence of melanomas. The mechanism behind this effect, however, is complicated—melanomas act differently depending on skin type, and do not always appear on the areas of skin most highly exposed to the sun. Curtin and co-workers report that there are a number of genetically different types of melanoma, each of which has differing degrees of susceptibility to UV light.

The researchers collected—from 7 international centers—126 archival, paraffin-embedded primary melanomas taken from skin with chronic sun-induced damage (primarily of the face; $n=30$), skin without chronic sun-induced damage (primarily of the trunk, arms and legs; $n=40$), ACRAL sites ($n=36$), and mucosal membranes ($n=20$). Differences in the number of copies of DNA in several genomic regions were evident in all four groups, and could be used to distinguish between the various types of melanoma with high accuracy. Important differences were also found in the frequency of mutations of specific genes; *BRAF* and *N-RAS* mutations were much more common in skin without chronic sun-induced damage than in the other groups, and strong interactions were found between *CDK4*, *CCND1*, *BRAF* and *N-RAS*. Chromosomal aberrations between the different types of melanoma were also apparent.

The authors state that their classification requires validation and further refinement. Their results, however, provide important evidence of distinct genetic pathways in the development of melanoma and suggest that patients might benefit from uniquely tailored therapies.

Pippa Murdie

Original article Curtin JA *et al.* (2005) Distinct sets of genetic alterations in melanoma. *N Engl J Med* **353:** 2135–2147

Pelvic irradiation increases the risk of pelvic fracture in elderly female cancer patients

Pelvic fractures are a major cause of mortality and morbidity among the aging female population. Radiation therapy for pelvic cancers can cause bone damage, which might increase the risk of bone fracture in elderly patients.

In a retrospective study using SEER PROGRAM data from 1986–1999, Baxter and colleagues investigated whether women with pelvic malignancies had increased risk of pelvic fracture following radiation therapy ($n=2,855$) compared with those who did not receive this treatment ($n=3,575$). The cumulative 5-year fracture rate was higher in women receiving radiation therapy than in those who did not undergo treatment. Using a proportional hazards model, the authors adjusted for confounding factors and showed that the risk of fracture following radiotherapy was associated with the site of cancer. Anal cancer patients had a higher risk of fracture than rectal or cervical cancer patients probably because of the close proximity of the femoral heads to the target nodes for radiotherapy.

No data were available on the radiation dosage or fields used in these patients, but modern techniques might reduce the exposure of bones to radiation relative to these earlier cases. Nevertheless, the study shows that radiation therapy is a considerable risk factor for fractures in elderly women with pelvic malignancies, and methods to minimize irradiation dose to the bone should be investigated. Targeted prevention strategies for reducing the risk of bone fracture in these patients need to be assessed in trials.

Kate Matthews

Original article Baxter NN *et al.* (2005) Risk of pelvic fractures in older women following pelvic irradiation. *JAMA* **294:** 2587–2593

Nucleophosmin mutation as a favorable prognostic marker in acute myeloid leukemia

The molecular chaperone nucleophosmin (NPM1) shuttles between the cytoplasm and the nucleus, transporting ribosomal proteins across the nuclear membrane. Mutations that result in NPM1 being trapped in the cytoplasm prevent NPM1 from carrying out its chaperone activity. Mutations in one section of the *NPM1* gene have been found in 35% of patients diagnosed with acute myeloid leukemia (AML), leading to the idea that AML development might be linked to these mutations. As other types of molecular abnormalities, such as internal tandem duplication (ITD) mutations in the fms-related tyrosine kinase-3 (*FLT3*) gene, have already been associated with prognosis, risk-stratification of individual cases of AML might be improved by