knowledge obtained from 'omics' techniques into clinical application, researchers are attempting to use microarrays — a means of analysing patterns of gene expression by looking at the mRNAs present — to determine the appropriate treatment for different patients. For instance, microarray profiling of breast tumours, using a set of 70 informative genes, has revealed gene-expression signatures that are associated with a good or a poor prognosis[1,2]. In these studies, roughly 40% of early-stage breast cancers turned out to have a 'good' signature, associated with only a 15% risk of metastasis (the spread of tumour cells) and a 5% risk of death by 10 years after diagnosis. According to current clinical practice, most patients with early-stage breast cancer receive adjuvant therapy (chemotherapy or endocrine therapy after surgery). But less than 1% of the patients with a 'good prognosis' signature would be likely to benefit, and the treatments often have harmful side effects (discussed by L. Van't Veer, Netherlands Cancer Institute, Amsterdam)[2]. So researchers now suggest using the 'poor' signature to guide the administration of adjuvant therapy to those for whom it would be most useful.

Indeed, gene-expression profiling is already being introduced clinically as a diagnostic procedure in academic centres in the Netherlands (L. Van't Veer), with similar programmes being launched in the United States. The profiles have been validated retrospectively in several cohorts of patients. Prospective validation, however, can only be achieved after 5–10 years. Also — as several speakers discussed — some technical issues have yet to be resolved, including how to procure and process samples and to ensure reproducibility and quality control. Nevertheless, various analysis platforms and short lists of diagnostic genes are being developed to predict the prognosis associated with other types of tumours, such as lymphomas (L. Staudt, NCI, Bethesda, and M. Piris, CNIO, Madrid), or to predict the likelihood of particular endpoints, such as metastasis (T. Golub, Broad Institute, Cambridge, Massachusetts). Predicting a patient's response to specific types of treatment would, of course, be the most important application. But it may take years for the approach to meet with regulatory approval and be extended from academic centres to mainstream practice.

Another strand of research involves the proteomic profiling of blood serum. This could soon complement — if not replace — the use of established tumour 'markers' in cancer screening and early diagnosis (E. Petricoin, FDA, Bethesda). Whereas specific tumour markers are often used singly, proteomic serum profiling involves the use of mass spectrometry to identify up to 15,000 peaks, representing proteins and protein fragments that are defined by their mass-to-charge ratios[3]. The sensitivity and specificity of such profiles has exceeded 90% for the diagnosis of lung cancer, and approached 100% for ovarian cancer (E. Petricoin). Most of the peaks have still to be identified, and several investigators argued that panels of specific immunoassays, which use antibodies that recognize particular proteins, should be developed for diagnosis instead. But it is the fragments, not intact proteins, that are often the most informative diagnostically, and there may be dozens — if not hundreds — of such fragments, possibly existing in complexes with one another and with other serum proteins. That makes the development of specific assays demanding.

A further application of proteomics concerns the analysis of signalling pathways, for example by studying the levels of specific phosphorylated proteins — a key feature of many pathways — in tumour samples (E. Petricoin). Analysis of these signalling profiles is being incorporated into many clinical trials to identify biological markers that indicate which tumours are likely to respond to treatment. Proteomic tumour profiling is often carried out from specific cell types, acquired by microdissection of the tumours. Such studies could also help us to understand the tumour microenvironment, where many different cell types and interactions may affect tumour behaviour. For example, in breast cancer, characteristics of the stromal fibroblast cells adjacent to the tumour might change, and contribute to, cancer progression (R. Weinberg, MIT) — much as does the growth of new blood vessels.

Moving on to studies of gene sequence (genomics), mutations in roughly 1% of human genes (291 genes in total) were reported to contribute to cancer (M. Stratton, Sanger Centre, Hinxton)[4]. Twenty-seven of these genes, more than would be expected by chance, encode protein kinases — enzymes that phosphorylate other pro-

Planetary science

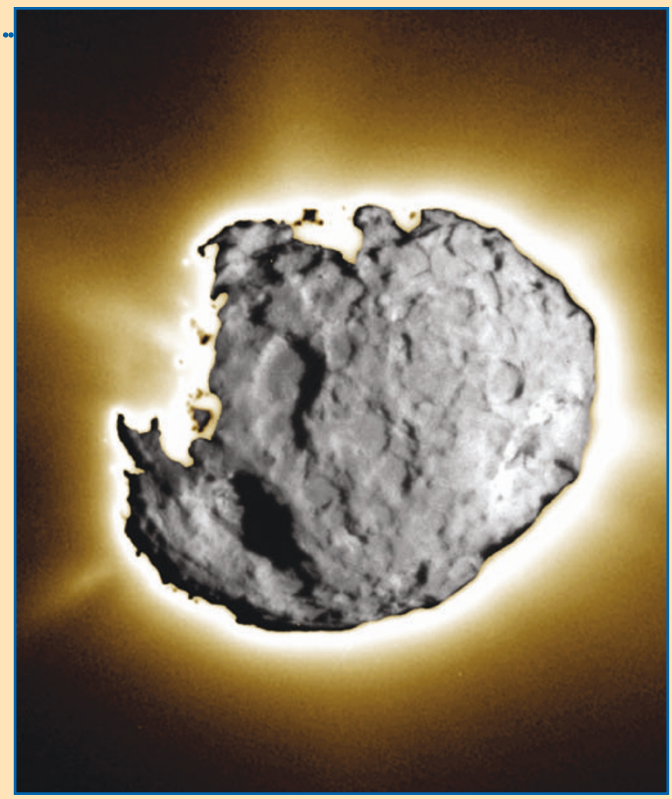
Stardust's comet memories

In January this year, NASA's Stardust spacecraft flew within 237 km of the comet Wild2. Stardust took 72 close-up shots during the flyby, described as an "unqualified success" at the Lunar and Planetary Science Conference in Houston, Texas, last week. After a few months' analysis, the Stardust team has now released stunning pictures of the comet's 5-km nucleus.

The Wild2 comet is 'fresh'. It is believed to have spent billions of years in the Kuiper belt, out beyond Neptune, until gravitational encounters kicked it into orbit closer to the Sun. In 1974, a close encounter with Jupiter knocked Wild2 into its present orbit, inside that planet's. Since then, Wild2 has passed close to the Sun only five times and so has suffered less exposure to solar radiation than other comets. Its surface bears a well-preserved record of its early history in the Kuiper belt.

The short-exposure image at the centre of this composite shows the cometary surface. The surface is markedly different from those of the comets Halley and Borrelly, and of Jupiter's ice-rich moons Callisto and Ganymede: instead of a continuum of crater size, Wild2's craters are mostly large; some are likely to be impact craters, others not. A long-exposure image taken 10 seconds later reveals a glowing halo of gas, thrown out from the nucleus in as many as 20 highly collimated jets.

Stardust's mission doesn't end there. The spacecraft is now heading for Earth once more, carrying particles from the comet's coma that were trapped during the flyby in centimetre-size aerogel cells. The samples will arrive on 15 January 2006. **Alison Wright**



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