IN THE NEWS

Abandoned survivors

A new report has criticized the haphazard nature of post-treatment care for the 10 million cancer survivors in the United States. Care is often inadequate because health plans only cover the initial cancer therapy, according to *From Cancer Patient to Cancer Survivor: Lost in Transition*, published by the National Academy of Sciences.

"We do a great job in addressing the acute need, but when patients get 3, 4, 5 years and beyond, they continue to experience issues and problems and may feel neglected" said Anne Meisner, of the Cancer Treatment Centers of America (http://www.bloomberg.com, 8 November 2005). These problems include not only recurrence, but also side effects of both cancer and therapy, such as depression, infertility, osteoporosis and leukaemia.

In addition, many people find themselves uninsurable or discriminated against at work. Janlori Goldman, of Columbia University, said, "Federal law is not entirely clear about whether employers can discriminate against a person who currently has cancer, has had cancer in the past or has a genetic predisposition to it" (http://www.ap.org, 7 November 2005).

The oncology community has welcomed the report, which addresses the angst of survivors such as Patricia Grullion, who said "I was given a clean bill of health, but nobody gave me any real plan for the future, or any thoughts about what I could expect physically or emotionally" (http://www.nytimes.com, 8 November 2005).

Patrick Goymer

IMMUNOTHERAPY

Do natural born killers specialize?

Natural killer T (NKT) cells can induce tumour regression in mouse models, but NKT cells can also suppress cell-mediated anti-tumour immune responses. The reason for these contrasting effects is not well understood. Now, Nadine Crowe and colleagues show that functionally distinct subsets of NKT cells exist *in vivo* and that their existence could help to explain why only some NKT cells have anti-tumour effects.

In previous studies, the authors showed that NKT cells derived from the liver can promote anti-tumour immune responses in two model systems: mice injected with the 3-methylcholanthrene-induced sarcoma cell line MCA-1, and mice injected with the melanoma cell line B16F10. Using these models, it was shown that mice that lack T-cell receptor (TCR) α-chains that contain Jα18 (denoted TCR Jα18), which are deficient in NKT cells, are more susceptible to tumour growth. In both tumour models, the ability of the NKT cells to promote anti-tumour responses was dependent on their production of interferon-γ. Previous reports have shown that there are at least two phenotypically distinct subsets of NKT cells in mice and humans — $CD4^+$ and $CD4^-$ NKT cells — and that these subsets show differential cytokine production *in vitro*. To test the idea that NKT-cell subsets are functionally distinct, as well as phenotypically distinct, the authors isolated NKT cells from the spleen, thymus and liver, then adoptively transferred these cells to TCR Jα18-deficient mice that had been injected with MCA-1 cells.

EPIGENETICS

Dangerous unmarked genes

Loss of imprinting (LOI) at specific loci has been implicated in several cases of tumorigenesis, probably as a result of imbalanced expression of potential imprinted tumour-suppressor genes and oncogenes. Previous studies have only demonstrated that LOI is associated with tumorigenesis, not that it causes it. Nor have they addressed the consequences of a global LOI, merely the consequences of single-gene LOI or imbalanced imprinting (having an entirely maternally or paternally imprinted genome). Now, Rudolf Jaenisch and colleagues have demonstrated that global LOI leads to tumour formation.

They used conditional mutants of DNA methyltransferase to transiently remove methylation from mouse embryonic stem (ES) cells. When methylation was restored, imprinting patterns were lost — the maternal and paternal genomes were no longer differentially methylated. The authors derived fibroblasts from these ES cells and found that they were immortalized, grew at an increased rate and resisted inhibition by transforming growth factor-β, a cytokine that inhibits the growth of various cell types.

Several tumour suppressors, such as *Igf2r*, *Tsp1* and *Cdkn1c*, were underexpressed in the fibroblasts, and oncogenes, such as *Peg3*, *Peg5* and *Igf2*, were overexpressed. When the non-imprinted fibroblasts were injected into immunodeficient mice there was some tumorigenesis, compared with none in the controls. However, when the fibroblasts were also transfected with constitutively active *RAS*, tumorigenesis was much faster. The authors suggest that this is because RAS and LOI cooperate to form tumours.

Chimeric mice that were created from a mixture of non-imprinted and normal ES cells all had tumours by 18 months of age, in contrast to the controls in which there was only one case of tumour formation. All the tumours in the chimeric mice were