IN THE NEWS

War against cancer

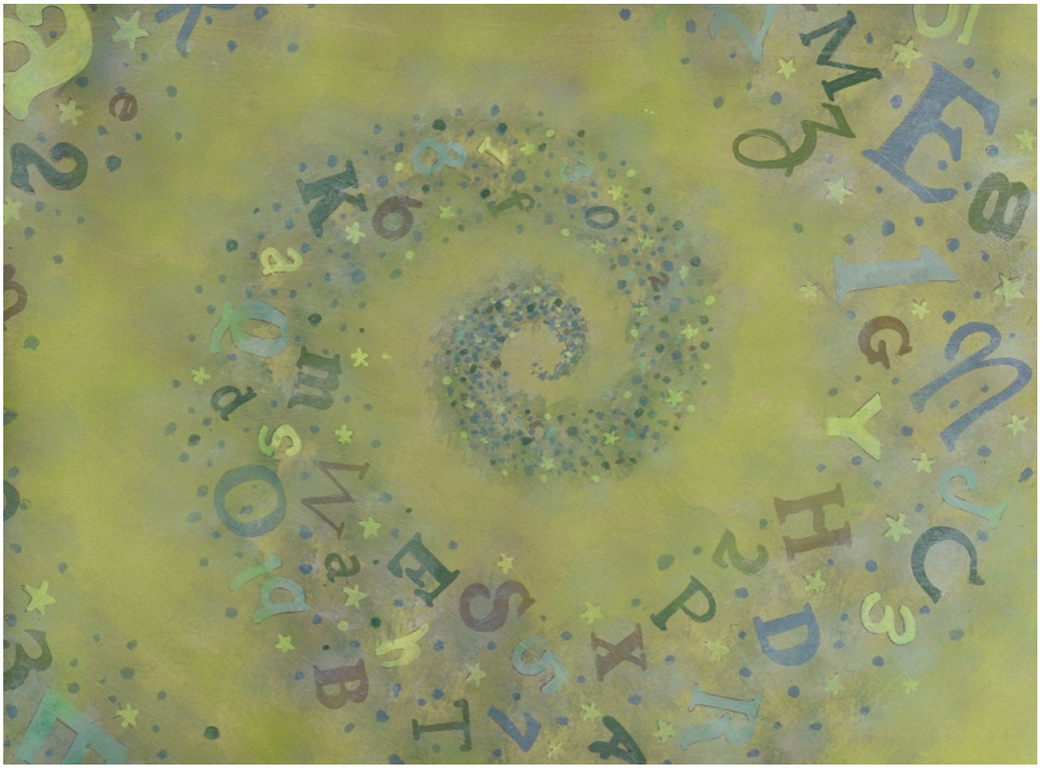
"Cancer: we're winning the war", proclaimed the *Daily Mail* UK in a full front-page feature on 4 July. This is obviously a little simplistic, but the report — from Sir Richard Doll and Sir Richard Peto (Cancer Research UK) — covered by this feature does show a dramatic drop in the number of deaths from lung cancer and breast cancer in the UK over the past 30 years.

In the 1960s, almost 250 men in every 100,000 per year in the UK died before the age of 70 from smoking-related diseases — today, the figure has more than halved to about 100 men per 100,000 per year. Richard Doll, who first discovered the link between smoking and lung cancer in the 1950s, said "We've been enormously successful at persuading people to quit…As a result, the death rate from lung cancer is tumbling more quickly than anywhere else in the world" (bbc.co.uk).

Deaths from breast cancer have also fallen significantly — 30% in the past decade. This decrease is due to improvements in both treatment and prevention of the disease — especially with the introduction of therapeutics such as tamoxifen — as well as increased early detection.

The two Sir Richards reported these results at the International Cancer Congress in Oslo in July, and were awarded the King Olav V's prize for Outstanding Cancer Research (www.oslo2002.org). Incidentally, Norway banned tobacco advertising more than 25 years ago — it is one of the few European countries to take such a step — and the death rate from lung cancer is considerably lower than the average for all developed countries.

Ezzie Hutchinson



ONCOGENESIS

A twist in the tale

Every good tale has a twist, and the fascinating story of c-MYC is no different. Dean Felsher and colleagues, reporting in the 5 July issue of *Science*, show that by briefly inactivating c-MYC, the cell's response changes from promoting life to promoting death, which has important implications for therapeutic strategies that target c-MYC.

Inactivating oncogenes would seem to be a sensible approach for treating cancer, but the toxicity that is associated with this can be high because most oncogenes are also essential for the growth of normal cells. Inactivating oncogenes for just a short period of time could solve the toxicity problem, but would tumours regrow following oncogene reactivation? The authors investigated this question by expressing c-*MYC* in mice lymphocytes behind the regulatable tetracycline promoter.

This mouse model has recently been shown to induce osteogenic sarcomas — apparently c-*MYC* is also expressed in immature osteoblasts — which share features with human osteogenic sarcomas, such as frequent metastasis. Switching off c-*MYC* by administering doxycycline caused the tumours to regress and the cells to differentiate into bone.

Culturing the osteogenic sarcoma cells *in vitro* allowed further analysis of the effects of switching off c-*MYC*. As expected, doxycycline treatment resulted in a rapid decrease in cell division; however, after removal of doxycycline and reactivation of c-MYC, cell division did not resume. Instead, cells underwent apoptosis — another event that is induced by c-MYC.

So does apoptosis also occur *in vivo*? Both primary tumours and osteogenic sarcomas that were transplanted subcutaneously into mice were investigated; doxycycline was administered after the tumours had reached a certain size. As expected, the tumour cells differentiated into osteocytes — mature bone cells. Reactivating c-MYC by removing doxycycline after 10 days resulted in a decrease in the number of cells by 14 days, and TUNEL staining confirmed that this was due to apoptosis. The tumours did not regrow.

Other reports have recently shown that the decision to live or die in response to c-MYC is determined by other genetic lesions — such as mutation of the apoptosis inhibitor *Bcl-x*$_L$ — so the ability of c-MYC alone to switch responses from proliferation to apoptosis is surprising and might be dependent on the cell type. Alternatively, the authors propose that inactivation of c-MYC, and the subsequent differentiation, might change the epigenetic context of the tumour cells, so that they are unable to evoke the proliferative response when c-MYC is reactivated.

So, a therapeutic strategy that temporarily inactivates oncogenes such as c-*MYC* might be both effective and have low toxicity. Whether this also works for different tumour types, metastatic tumours and even human tumours remains to be determined.

Emma Greenwood

References and links

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FURTHER READING Weinstein, I. B. Addiction to oncogenes — the achilles heal of cancer. *Science* **297**, 63–64 (2002) | Felsher, D. W. & Bishop, J. M. Reversible tumorigenesis by *MYC* in hematopoietic lineages. *Mol. Cell* **4**, 199–207 (1999)
WEB SITE
Dean Felsher's lab: http://ccis.stanford.edu/peoplepages/felsher/felsher1.htm