IN THE NEWS

Time for a change?
The aromatase inhibitor anastrozole (Arimidex) is a more effective treatment for post-menopausal women with breast cancer than the current gold standard tamoxifen, delegates were told at the San Antonio Breast Cancer Symposium in Texas.

Anthony Howell (Manchester, UK), who presented the findings of the Arimidex, Tamoxifen alone or in combination (ATAC) trial, which show that anastrozole increases the time to cancer recurrence by 20% and cuts the chances of breast cancer arising in the other breast by 40%, said "I think this is an important study because if we prevent recurrences, this will translate into improvements in survival" (http://www.guardian.co.uk, 8 December 2004).

However, these findings raise financial worries for the National Health Service in the UK, where the drug is not currently licensed. Anastrozole is considerably more expensive than tamoxifen and, with 100,000 women taking tamoxifen at any one time in the UK, the switch could cost nearly £100m.

A spokesperson for AstraZeneca, the manufacturer of both tamoxifen and anastrozole, said that they will reduce the price of anastrozole in the UK, making it more likely that it will be licensed for use by all women who are eligible for it. (http://reutershealth.com, 8 December 2004).

Other experts warned that further studies were still needed before changing the standard treatment. "We should be careful not to rush to judgement as to what the best way should be to use these drugs", said Eric Winer of the Dana-Farber Cancer Institute in Boston. (http://seattletimes.nwsource.com, 9 December 2004).

Nicola McCarthy

STEM CELLS

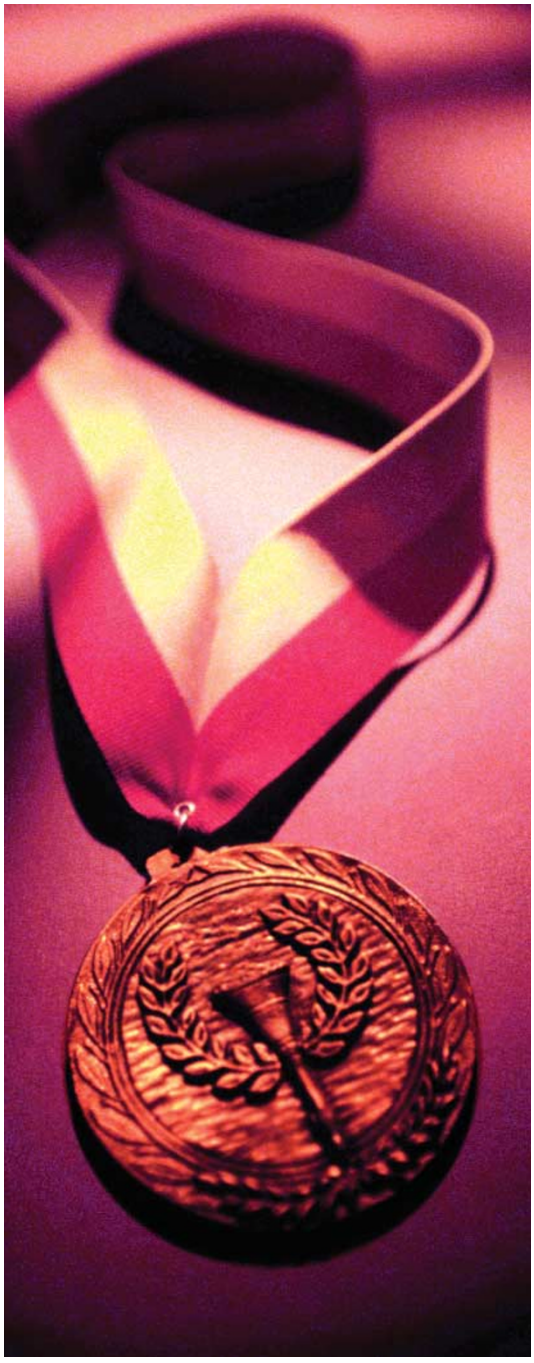
First and foremost

The cancer stem-cell hypothesis proposes that tumours are populated by a rare fraction of cells with stem-cell properties. Although cancer stem cells have been identified and characterized in leukaemias, there is only a small amount of evidence for their existence in solid tumours. Peter Dirks and colleagues report the isolation and characterization of a cell subpopulation from human brain tumours that have stem-cell properties *in vivo*.

Cancer stem cells are identified based on their ability to undergo self-renewal, as well as the ability of small numbers of these cells to form tumours with the same phenotype as the tumour they were derived from. Dirks and colleagues had previously identified a population of human brain tumour cells, isolated either from aggressive glioblastomas or medulloblastomas, with *in vitro* stem-cell-like properties. Cells from both tumour types where characterized by expression of the cell-surface glycoprotein CD133, which is also expressed by normal neural and haematopoietic stem and progenitor cells. In a study recently published in *Nature*, they describe the *in vivo* capabilities of these cells following injection into non-obese diabetic/severe combined immunodeficient (NOD/SCID) mice. Injection of as few as 100 $CD133^+$ cells produced a tumour that had the same characteristics as the patient's original tumour. Injection of up to 10^5 $CD133^-$ cells, however, did not cause tumour formation in these mice, indicating that $CD133^+$ cells are the brain tumour stem cells.

What are the characteristics of these stem cells? In addition to their high rates of proliferation, both medulloblastoma and glioblastoma $CD133^+$ cells expressed neural precursor markers, which $CD133^-$ cells did not. Instead, $CD133^-$ cells express differentiated neural lineage markers. This indicates that these cancer stem cells have taken on neural precursor phenotypes. $CD133^+$ cells also had a key property of cancer stem cells — self-renewal capacity in serial re-transplantation assays. When as few as 1,000 $CD133^+$ cells from original xenografts of both brain tumour types were re-injected into a second set of mice, these mice formed brain tumours with the same phenotype of the primary xenograft.

Both $CD133^+$ and $CD133^-$ tumour cell types had the same cytogenetic alterations, indicating that they were derived from the same original clone. The $CD133^+$ cells only make up about 20–30% of the overall tumour population, however, and the authors propose that these cells have somehow acquired patterns of abnormal differentiation. Further experiments will determine whether this stem-cell-initiating event occurs in a normal stem cell, or in normal progenitor/differentiated cells that have re-acquired stem-cell properties. Also, since only a small population of cancer cells appears to be capable of regenerating an entire tumour, treatment relapse is likely to be the result of failure to target the tumour-initiating cell.



Kristine Novak

References and links

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FURTHER READING Pardal, R., Clarke, M. F. & Morrison, S. J. Applying the principles of stem-cell biology to cancer. *Nature Rev. Cancer* **3**, 895–902 (2003)
WEB SITE
Peter Dirks' lab: http://www.sickkids.ca/BTRC/section.asp?s=BTRC+Laboratories&sID=289&ss=Dirks+Lab&ssID=304