IN THE NEWS

Be sun-smart

The incidence of non-melanoma skin cancer has nearly tripled in women under the age of 40, according to a US study (Christenson, L. J. *et al*. *JAMA* **294**, 681–690 (2005)).

Non-melanoma skin cancer usually occurs in the over 50s but little is known about its incidence in younger people. So, the authors analysed incidence data from 417 people younger than 40 years diagnosed with non-melanoma skin cancer between 1976 and 2003. The rate of basal cell carcinoma rose from 18.2 out of 100,000 in 1976–1979 to 29.1 out of 100,000 in 2000–2003. The incidence of squamous cell carcinoma also rose from 0.9 out of 100,000 to 4.1 out of 100,000 over the same time period. The increase in non-melanoma skin cancer was particularly marked in women in their late 30s. "We have discovered that these cancers are becoming increasingly prevalent in younger people, and if steps are not taken at a young age to prevent these cancers, we may see an exponential increase in the overall occurrence of non-melanoma skin cancers", said lead researcher Leslie Christenson of the Mayo Clinic, Minnesota (http://www.bbc.co.uk, 9 August 2005).

The researchers warned that a tan is still considered a sign of health and beauty despite the harm it can cause, and that this view has to change (http://www.reutershealth.com, 10 August 2005). The head of health information at Cancer Research UK, Sara Hiom, said "[Our] SunSmart campaign says that people should avoid burning by seeking shade when the sun is at its height, covering up in a T-shirt, hat and sunglasses and applying factor 15-plus sunscreen" (http://www.bbc.co.uk, 9 August 2005).

Ezzie Hutchinson

SENESCENCE

In vivo veritas

Studies in cultured cell lines have shown that oncogene-induced senescence is an important guardian against transformation, but the role of senescence in *in vivo* tumour formation has not been established. Four papers published in *Nature* have laid this issue to rest, demonstrating that senescence protects against tumour progression in animal models and in human tissues.

Characterized by the stable growth arrest that occurs in response to various cell stressors, including oncogene induction, senescence is known to be regulated by the ARF–p53 and also the INK4A–RB (retinoblastoma protein) signalling pathways. Chrysilis Michaloglou *et al.* investigated senescence in human naevi (moles), which are benign tumours of melanocytes that frequently carry activating mutations in the oncogene *BRAF*. Naevi remain in a growth-arrested state for decades, and only rarely progress into malignancy (melanoma). Michaloglou *et al.* showed that mutant BRAF-expressing naevi also express high levels of senescence markers and do not proliferate. This is because activated BRAF cannot fully transform human melanocytes — additional mutations are required to disable the senescence machinery, allowing melanomas to arise. Not all naevi cells upregulate INK4A, ARF or p53, however, indicating that other, undiscovered senescence-inducing mechanisms exist in human melanocytes.

In another article, Zhenbang Chen *et al.* showed that senescent cells are also present in early-stage prostate cancers of both humans and mice. In mouse prostate cells, inactivation of the tumour-suppressor PTEN (phosphate and tensin homologue) leads to senescence through a p53-dependent pathway, both *in vitro* and *in vivo*. Loss of both PTEN and p53, however, results in the rapid formation of invasive prostate cancer. So p53-mediated senescence induction seems to be a protective mechanism against prostate tumour progression.

One of the limitations of studying senescent cells in tumours has been the limited number of markers available. Using a microarray screen, Manuel Collado *et al.* identified a small set of genes for which the expression level was correlated with senescence induction. Using a combined panel of markers, his group analyzed the distribution of senescent cells in various activated RAS-induced tumours in mice. They showed that senescent cells uniformly exist in pre-malignant tumours, but not in malignant ones, and conclude that oncogene-induced senescence helps to restrict tumour progression.

Melanie Braig *et al.* investigated a novel mechanism of senescence induction in response to oncogenic RAS. Transgenic mice that express activated RAS in their haematopoietic cell compartment (Eμ-*NRas* mice) develop non-lymphoid neoplasia after long periods of time, with most cells undergoing senescence through an RB-mediated pathway. Previous reports of the presence of heterochromatin foci in senescent cells indicated that histone modifications were associated with growth arrest. Since the histone methyltransferase SUV39H1 binds to RB, the authors investigated whether these two proteins function together to regulate senescence. Indeed, Eμ-*NRas* mice with targeted deletions of *Suv39h1* rapidly succumbed to invasive T-cell lymphomas, indicating that this protein is an important inhibitor of lymphoma progression. The authors propose that SUV39H1 and RB might somehow regulate the DNA packaging required for senescence.

Together, these studies show that although senescence induction is a highly heterogenous process, it seems to be a universal barrier against tumour progression. Further studies are required to determine the exact pathways that trigger senescence when oncogenes become activated, and how some cells escape senescence to progress into highly invasive, metastatic tumours.

Kristine Novak

References and links

ORIGINAL RESEARCH PAPERS Michaloglou, C. *et al*. $BRAF^{E600}$-associated senescence-like cell cycle arrest of human naevi. *Nature* **436**, 720–724 (2005) | Chen, Z. *et al*. Crucial role of p53-dependent cellular senescence in suppression of Pten-deficient tumorigenesis. *Nature* **436**, 725–730 (2005) | Collado, M. *et al*. Senescence in premalignant tumours. *Nature* **436**, 642 (2005) | Braig, M. *et al.* Oncogene-induced senescence as an initial barrier in lymphoma development. *Nature* **436**, 660–665 (2005)

FURTHER READING

Schmitt, C. A. Senescence, apoptosis and therapy — cutting the lifelines of cancer. *Nature Rev. Cancer* **3**, 286–295 (2003)