# In the news

## POOR DEVILS

The facial tumours that have decimated the Tasmanian Devil population are infectious and derive from a single animal, according to research published in *Nature* (http://www.nature.com, 2 February 2006).

In the past 10 years the population of these carnivorous marsupials has decreased from 140,000 to 80,000 because of a facial tumour that causes starvation. The new research proposes that it is the animals' vicious behaviour that is to blame. "Devils jaw wrestle and bite each other a lot…and bits of tumour break off one devil and stick in the wounds of another" said the study's author, Anne-Marie Pearse (http://news.bbc.co.uk, 2 February 2006). She added "It occurred to me that there didn't necessarily have to be a virus if the [cancer] cells themselves could be transmitted" (http://www.sciencenews.org, 2 February 2006).

The evidence that the tumours are infectious and derive from a single source came from examining karyotypes. The authors found exactly the same complex set of chromosomal rearrangements in the tumours of all 11 animals that they studied. In addition, one animal had a chromosomal rearrangement in its normal cells that was not found in its tumour. This identical tumour karyotype, found at all stages of tumour development and in all individuals, strongly supports the infectious theory.

It is thought that the low genetic diversity of the devils is the reason that the immune system does not kill the foreign cancer cells. A similar phenomenon has been observed when cancer cells are inadvertently transmitted with donated organs between closely related individuals.

A cull of infected animals is now thought to be the best way to proceed. "This is an incredibly urgent problem" said Ian Campbell, the Australian Environment Minister, announcing increased funding (http://www.abc.net.au.com, 7 February 2006).

*Patrick Goymer*

SIGNALLING PATHWAYS

# A flying start

> "the Notch pathway collaborates with epigenetic-silencing pathways and cell-cycle control in tumour development"

Activation of conserved developmental signalling pathways, such as Notch, has been observed in human cancers, but activation of such pathways in animal models seems to be insufficient for tumorigenesis. Ferres-Marco *et al.* now report that in a *Drosophila melanogaster* model the Notch pathway collaborates with epigenetic-silencing pathways and cell-cycle control in tumour development.

The developing eye in *Drosophila* is a good model for identifying tumour-inducing mechanisms because it is simple and genetically well-defined. The growth of the eye depends on Notch activation by its ligands Delta and Serrate. The 'large eye' phenotype model, produced by overexpression of *Delta* (see figure), was screened by upregulating genes at random and looking for induced tumour growth. Ferres-Marco and colleagues found that overexpression of two neighbouring genes, longitudinals lacking (*lola*) and pipsqueak (*psq*) caused tumour formation (see figure). Both Psq and Lola behave as epigenetic silencers of the Polycomb group, which maintain transcriptional repression patterns.

So, do *psq* and *lola* contribute to the tumour phenotype when co-activated with the Notch pathway? The authors introduced point mutations into these genes to disrupt their expression — all $psq^-$ mutations prevented tumorigenesis and all $lola^-$ mutations reduced eye-tumour size. Most of the mutations were in the BTB domain of *Psq*, and, as BTB-protein-family members are transcriptional repressors and include oncogenes that recruit Polycomb proteins, the authors speculated that deregulated *psq* and *lola* could lead to tumorigenesis by epigenetic

TUMORIGENESIS

# Culpable kinase

> "CDK4 might prove to be a selective therapeutic target in all tumours that overexpress ERBB2"

Cyclin-dependent kinase 4 (CDK4) has been implicated as a potential new therapeutic target in women with breast cancers that overexpress ERBB2 and cyclin D1.

CDK4 regulates cell-cycle progression by interacting with the D-type cyclins and phosphorylating and inhibiting the retinoblastoma protein (RB). Cyclin D1 is overexpressed in many cancers, including most breast cancers, and loss of this protein is known to suppress mammary carcinogenesis in mouse models. However, whether this is dependent on the kinase activity of the cyclin D1–CDK4 complex or on cyclin-D1 kinase-independent functions was unclear, so Yu and colleagues investigated.

To check whether CDK4 activity was required for breast development, the authors used a mouse model in which cleared mammary fat pads were transplanted with either *Cdk4*-null mammary epithelium or wild-type mammary epithelium. All of the transplanted mice developed normal breast architecture during pregnancy and were able to lactate, supporting the