BEHAVIOURAL GENETICS

A question of grooming

If you own a cat, you'll know how much time they spend preening themselves. Rather than a bad case of narcissism, this represents a type of grooming behaviour, which is essential to the well-being of most animals. But, like most things, it can go wrong. In humans, defective grooming behaviour ranges from the mild, such as nail-biting, to the severe, such as the obsessive–compulsive disorder trichotillomania (compulsive hair pulling that results in hair loss). Little is known about the genetics that underlie grooming behaviours, but Greer and Capecchi now report that mice with null mutations in the homeobox gene *Hoxb8* groom excessively, potentially providing researchers with a valuable model for studying abnormal grooming behaviour in humans.

The authors constructed a null mutation in *Hoxb8* by inserting a frameshift mutation in exon 1 and a *neo* gene, surrounded by *lox*P elements, in exon 2. They then removed the *neo* gene by inducing Cre-mediated recombination, to produce an allele with nonsense codons in both exons. The removal of *neo* turned out to be very important because when *neo* was retained, a skeletal phenotype was seen in homozygous mutant mice. This was most likely because the presence of *neo* causes the aberrant expression of nearby genes in the Hoxb cluster.

In the absence of *neo*, bald patches (sometimes accompanied by skin lesions) were the only other phenotype in *Hoxb8*$^{-/-}$ mice. There was no obvious skin defect to account for this, so the authors videoed the mutant mice for 24 h to see whether they showed any behavioural abnormalities. Strikingly, they found that the mutants spend twice as long grooming themselves as their wild-type littermates. This excessive licking and biting leads to the loss of body hair and to skin lesions. Furthermore, the mutants also excessively groom normal mice in the same cage, indicating that the behaviour is not the result of some abnormality in the skin of the mutant mice — rather it is a defect in grooming behaviour itself.

Greer and Capecchi also studied the expression of *Hoxb8* and found high levels of expression in several parts of the brain that had been previously implicated in grooming behaviour in several mammals. Imaging studies have also detected abnormalities in the same brain regions in patients with obsessive–compulsive disorder, which fits with the similarity in phenotype between trichotillomania and the *Hoxb8* mutants. This work therefore provides a valuable way into the biology that underlies grooming behaviour. The search will now be on to see whether variation in *HOXB8* itself accounts for any of the variation in grooming behaviour in humans.

Mark Patterson

References and links

ORIGINAL RESEARCH PAPER Greer, J. M. & Capecchi, M. R. Hoxb8 is required for normal grooming behavior in mice. *Neuron* **33**, 23–34 (2002)

WEB SITES

Trichotillomania Learning Center: http://www.trich.org/

Mario Capecchi's lab: http://www.genetics.utah.edu/section2/sc205frm.html

IN BRIEF

DEVELOPMENTAL BIOLOGY

The novel zinc finger-containing transcription factor Osterix is required for osteoblast differentiation and bone formation.

Nakashima, K. *et al. Cell* **108**, 17–29 (2002)

Osteoblasts are involved in bone formation during development, as well as in bone repair and maintenance later in life. In a cDNA screen for osteoblast-specific transcription factors, Nakashima and colleagues identified a zinc-finger protein, Osterix, which when knocked out in mice results in initial cartilage formation, but a failure to form bones. The authors show that this is caused by a failure of osteoblasts to differentiate and conclude that Osterix is specifically required in this process.

GENOMICS

The genome of the natural genetic engineer *Agrobacterium tumefaciens* C58.

Wood, D. W. *et al. Science* **294**, 2317–2323 (2001)

Genome sequence of the plant pathogen and biotechnology agent *Agrobacterium tumefaciens* C58.

Goodner, B. *et al. Science* **294**, 2323–2328 (2001)

The common soil microbe *Agrobacterium tumefaciens* causes serious agronomic losses by causing crown gall in plants. To plant researchers, this property of infecting and transferring genetic material is a boon, and for 25 years the microbe's Ti plasmid has been engineered to deliver transgenes to plants, as well as to fungi and human cells. Now, two groups have independently sequenced the 5.67-Mb genome of the experimentally most popular strain, C58, which contains a linear and a circular genome, as well as two plasmids. The type and organization of the organism's 5,400 genes indicate that *Agrobacterium* might share a common ancestor with benign plant symbionts of the same class. Further studies will no doubt improve our ability to harness this 'natural genetic engineer'.

MOUSE MODELS

Development of spontaneous airway changes consistent with human asthma in mice lacking T-bet.

Finotto, S. *et al. Science* **295**, 336–338 (2002)

The incidence of asthma — an allergic condition characterized by inflammation of the airways — is on the increase, and so there is a strong incentive to develop animal models of the condition that can reveal potential therapeutic targets. Prompted by the observation that the expression of *T-bet*, which encodes a T-box transcription factor, is reduced in the lungs of asthmatic patients, the authors knocked out the homologous gene in mouse. *T-bet*$^{+/-}$ and *T-bet*$^{-/-}$ mice recapitulated the phenotype of both acute and chronic human asthma, even without exposure to allergen. Intriguingly, mouse *T-bet* maps to a genetic region on chromosome 11 that has been linked to asthma in mice and humans.