exploited the short LD across dog breeds to fine map the locus for the second trait, the hair ridge. This dominant trait is caused by a duplication that includes three fibroblast growth factor genes. The involvement of developmental genes could explain the high incidence of a neural tube defect in ridged dogs.

Association mapping of simple phenotypes in dogs is therefore both feasible and can be done unambiguously with only a few individuals. The authors predict that it could take as few as 200 dogs to fine map genes that convey a three- to fivefold increased disease risk, raising the hope that the approach can be extended to map complex traits.

Tanita Casci

ORIGINAL RESEARCH PAPERS
Karlsson, E. K. *et al.* Efficient mapping of Mendelian traits in dogs through genome-wide association. *Nature Genet.* 30 September 2007 (doi:10.1038/ng.2007.10) |
Salmon Hillbertz, N. H. C. *et al.* Duplication of *FGF3*, *FGF4*, *FGF19* and *ORAOV1* causes hair ridge and predisposition to dermoid sinus in Ridgeback dogs. *Nature Genet.* 30 September 2007 (doi:10.1038/ng.2007.4)

equivalent derepression of the *sal* CRE, and loss of binding of either component did not affect that of the other — so MED–MAD and UBX are equally required, rather than acting additively. However, there was no evidence for a physical interaction between MED–MAD–SHN and UBX, and moving the UBX binding sites away from the MED–MAD site similarly abolished repression of *sal*1.1. Comparison of the *sal* CRE between *Drosophila* species revealed a perfectly conserved 37-bp region encompassing the binding sites — striking evidence that this strict topology has been evolutionarily conserved.

The authors suggest that, rather than being master regulators, Hox proteins might generally rely on collaborations with cofactors that are actually responsible for directing gene expression, a mechanism that could be far more widespread previously thought.

Carrie Patis

ORIGINAL RESEARCH PAPER Walsh, C. M. & Carroll, S. B. Collaboration between Smads and a Hox protein in target gene repression. *Development* **134**, 3585–3592 (2007)

CHROMATIN

Remodellers are more than just muscle

Shifting nucleosomes along DNA is an essential part of gene expression in eukaryotes — it allows regulatory proteins to gain access to previously inaccessible sequences. Although this nucleosome relocation is known to be the job of ATP-dependent chromatin remodellers, uncertainty has surrounded the question of whether these proteins are specific in terms of the sites to which they move nucleosomes. An investigation of mammalian remodellers now provides evidence that these proteins do show such specificity, and that this is directed by the sequence of the DNA substrate.

If repositioning by remodellers is determined simply by which DNA sequences have the highest affinity for nucleosomes, then, for a particular substrate, different remodellers should relocate nucleosomes to the same high-affinity positions. Rippe, Schrader and colleagues tested this possibility *in vitro* for seven mammalian remodelling complexes on two DNA substrates: the heat shock protein 70 (*hsp70*) fragment from *Drosophila melanogaster* and the mouse ribosomal DNA (rDNA) promoter. Following repositioning by the remodellers, relocation was indeed mainly to sites with high affinities for nucleosomes. However, the seven complexes gave distinct patterns in terms of which combination of these sites were occupied — evidence that the remodellers themselves have a role in determining the new location of nucleosomes.

One potential explanation for this remodeller specificity is that the enzymes are directed by DNA sequence information. On the rDNA substrate, one site of nucleosome positioning by the ACF chromatin-remodelling complex is strongly correlated with a DNA region that is intrinsically curved, with the repositioned nucleosome centred close to the peak of the curvature. The authors took a 40-bp fragment that spanned this peak and moved it into a new sequence environment. As in the rDNA context, ACF positioned a nucleosome close to the curvature peak, and the same result was found when the 40-bp sequence was placed into two other sequence environments. So, it seems that nucleosome repositioning is indeed directed by DNA sequence elements.

Finally, the authors tested two models for how such elements might direct remodellers. One possibility is that the enzyme is released at a particular position because of a low binding affinity for the sequence, thus determining the relocation end point (the 'release model'). Alternatively, the end point could be specified by the remodeller moving into a region that provides a poor substrate for the translocation of the enzyme, so that the remodeller comes to a standstill (the 'arrest model'). In the case of the remodellers chromodomain helicase DNA-binding protein 1 (CHD1) and ACF, among the potential sites of occupancy, nucleosomes were repositioned to the sites with the lowest binding affinity for the enzyme — consistent with the release model.

So, it seems that ATP-dependent chromatin remodellers do more than just providing the brawn when it comes to nucleosome positioning. The diversity of these enzymes and the complexes that they participate in suggest that their repositioning specificity provides an important level of gene regulation.

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ORIGINAL RESEARCH PAPER Rippe, K. *et al.* DNA sequence- and conformation-directed positioning of nucleosomes by chromatin-remodeling complexes. *Proc. Natl Acad. Sci. USA* 24 September 2007 (doi: 10.1073/pnas.0702430104)
FURTHER READING de la Serna, I. L., Ohkawa, Y. & Imbalzano, A. N. Chromatin remodelling in mammalian differentiation: lessons from ATP-dependent remodellers. *Nature Rev. Genet.* **7**, 461–473 (2006)
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