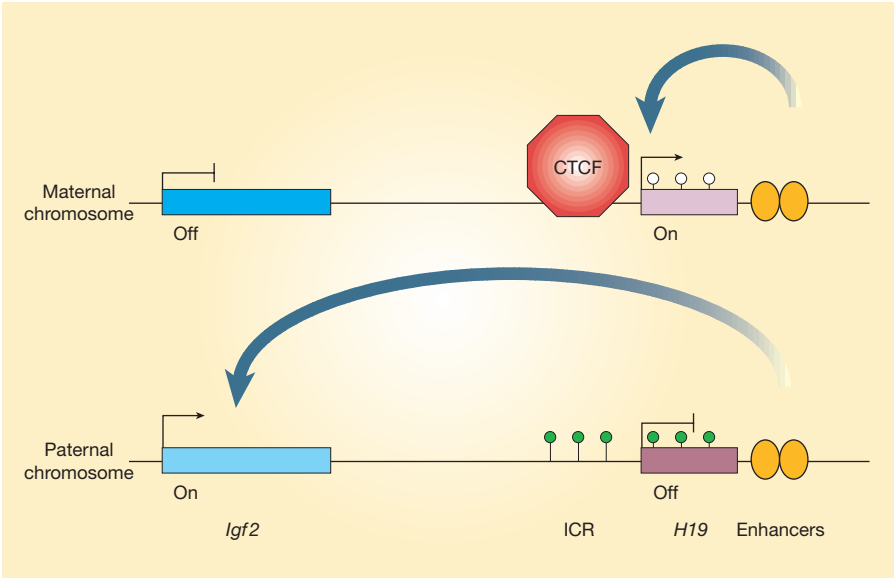

Figure 1 **Selective gene silencing by boundaries. *H19* and *Igf2* are genes that are expressed from only the maternal or the paternal chromosome. *H19* is expressed from the maternal chromosome only; *Igf2* is expressed only from the paternal chromosome. The two genes share an enhancer region, located downstream of *H19*. The new papers[1–4] show that the ICR (imprinting-control region) of *H19* is a boundary element, controlled by DNA methylation. The CTCF protein binds to the unmethylated maternal ICR. This prevents the promoters located in the *Igf2* gene from interacting with the enhancers downstream of the *H19* gene, resulting in transcriptional silencing of *Igf2*. The paternal ICR is methylated (filled circles), preventing binding of CTCF. This allows the enhancers to contact the promoters of the paternal *Igf2*, allowing the gene to be transcribed. The paternal *H19* gene is thought to be silenced by methylation. Differentially methylated regions are also found in *Igf2*, but are not shown here.**

CTCF do? First we need to take a step back and look at the way in which enhancers and promoters interact to control gene expression. These two control regions may work together in one of two ways. One way involves the 'tracking' of transcription complexes from the enhancers, along the DNA, to the promoter. Alternatively, the DNA may loop round such that the enhancers and promoters interact. The *Igf2* promoters are about 100 kilobases from the enhancers, so the looping model seems more attractive. On the maternal chromosome, either looping or the interaction between the promoters and the enhancers could be disrupted by CTCF (and possibly other factors) binding to the ICR. In addition, binding of CTCF and other factors could have a role in opening the chromatin of the *H19* gene for transcription — CTCF has been implicated in gene activation as well as repression (Box 1).

Indeed, the *H19* ICR seems to have many other functions as well as being a boundary. For example, it is needed for methylation of the paternal *H19* gene[9], and for silencing of this gene independently of methylation[12]. The region seems to contain many functional elements that are involved in regional regulation of methylation, in silencing and in insulating. Other functions may be revealed by further study of these elements and of the protein and chromatin factors that bind to them.

Does the discovery of the epigenetic boundary upstream of *H19* bring to an end the search for the regulators of *H19* and *Igf2*? Probably not — the fact that deletion of the ICR only partially activates the maternal *Igf2* gene[9] indicates that other sequences may be involved in keeping the silence. Indeed, deletion of a silencer that is also controlled by methylation and is upstream of *Igf2* also activates the silent *Igf2* allele (M. Constancia *et al.*, unpublished observations). The imprinting arsenal includes promoters, enhancers, antisense RNA transcripts[13], silencers and chromatin boundaries. What is fascinating is that these sequences have come under epigenetic control. ■

Wolf Reik and Adele Murrell are in the Laboratory of Developmental Genetics and Imprinting, The Babraham Institute, Cambridge CB2 4AT, UK.
e-mail: wolf.reik@bbsrc.ac.uk

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100 YEARS AGO

Possibly some of your photographer readers may be glad to know that microphotography of sorts is within the reach of all who possess a microscope with suitable substage-condenser and a camera… One of my earliest attempts was to photograph fluid inclusions in quartzes with ordinary sunlight, and rock sections polarised. The only difficulty was that the sun would not keep still, and without a heliostat the work was most troublesome, not to say aggravating. In one case, a mere movement of the condenser-diaphragm made the bubble in the inclusion fly backwards and forwards… With a little device in the double lantern the motion of bubbles in inclusions can be shown on a nine-foot screen. These negatives were taken with a 1/16th immersion, the camera being extended with a brown paper tube, and the extra apparatus did not cost one shilling… While observing the transit of Venus, I thought I would try a photograph. I drilled a hole in the telescope cap for diaphragm; took off the eye-piece and stuffed the telescope into a common camera, with a red cloth to make it light-tight; exposed six negatives with hand exposure on instantaneous plates. Result: four passable negatives and one good one. This quite unlooked-for success was due to some back volumes of *Nature* which propped up the camera.
From *Nature* 24 May 1900.

50 YEARS AGO

Twilight in India

This book is well named, for the author has a very dim view of India. In spite of a good deal of interesting and, on the whole, well-informed matter on south Indian castes, the whole book is coloured by an obvious determination to view everything Hindu in the darkest shadow, and all the less creditable aspects of Hinduism, particularly in regard to sex, are enlarged on at the expense of its merits.

There is obviously a good deal of exaggeration in many of the statements made, for the meriah sacrifice is written of — and that in 1949 — as if it continued as a routine ceremonial. Several of the illustrations are borrowed without acknowledgement from Thurston; and, although misprints abound, the fact that "tumeric" is repeatedly used for "turmeric" suggests that possibly it is not the printer who is to blame for "foistered" instead of "foisted" — or perhaps "fostered".
From *Nature* 27 May 1950.