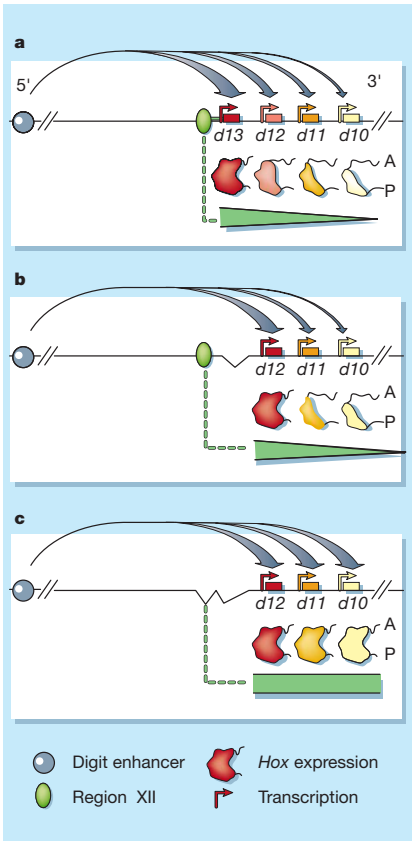

Figure 1 **Regulating gene clusters in future fingers and toes. Kmita *et al.*[5] have studied the expression of the *Hoxd13* to *Hoxd10* (*d13* to *d10*) genes in developing mouse limbs.** a, **The normal expression pattern, which results in normal digit development. These *Hox* genes were already known to be expressed in a quantitatively collinear way (green triangle), with *Hoxd13* expressed at the highest levels and most anteriorly in the future fingers and toes, and *Hoxd10* expressed least and posteriorly. A region that enhances *HoxD* transcription, the digit enhancer, is located at least 100,000 bases 5′ to the gene cluster. The thickness of the black arrows shows the strength of enhancement. Kmita *et al.* have also identified another control element, region XII, that interacts with the digit enhancer.** b, **The authors show that deletion of *Hoxd13* strongly enhances *Hoxd12* expression, resulting in a *Hoxd13*-like pattern. *Hoxd12* takes over the function of *Hoxd13*.** c, **Deletion of *Hoxd13* together with region XII abrogates quantitative collinearity. A, anterior; P, posterior.**

deletion of region XII alone has no effect, which reveals redundancy among the nearby regulatory elements.

During limb development, then, quantitative collinearity is established by interactions of the remote digit enhancer with regulatory elements located at the 5′ border of the *HoxD* cluster. These interactions seem to have the strongest effect on the 5′-most gene — normally *Hoxd13* — and progressively weaker effects on more 3′ genes (*Hoxd12* to *Hoxd10*). It is unclear, however, whether it is strictly essential for digit development that *Hoxd13* is expressed at the highest levels and most anteriorly, and *Hoxd12* to *Hoxd10* at progressively lower levels; or whether it is simply that a leaky 'first come, first served' mechanism ensures high expression of *Hoxd13* in future digits.

The results of Kmita *et al.*[5] are somewhat reminiscent of how the locus control region (LCR) regulates the cluster of β-globin genes[9], which encode blood proteins that are involved in oxygen transport and storage during development and in adults. In both cases, the order of genes within the cluster is essential for their correct regulation by a remote enhancer, although the LCR activity is more sensitive to control elements that are specific to individual genes than is the digit enhancer.

It will be interesting to see whether the mechanism uncovered by Kmita *et al.* is unique to the 5′ *HoxD* genes, or whether it is also used by other gene clusters to achieve new types of tissue-specific regulation. Another question is how frequently remote enhancers have been recruited to alter the expression of existing genes during the evolution of new body structures in vertebrates. One example concerns the *Sonic hedgehog* gene, which is essential for digit patterning — its limb-bud-specific expression is controlled by regulatory elements located a staggering 800 million bases 5′ to the protein-coding region[10]. The next task will be to identify the precise molecular mechanisms that underpin long-distance concerted regulatory interactions, and the factors involved. This will be a challenge, but promises much excitement for the future. ■

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100 YEARS AGO

The utilisation of the internal heat of the earth has often been suggested as an engineering problem of the future. The Rev. E. Rattenbury Hodges directs our attention to an issue of the *Boston News Bureau* in which a scheme is seriously proposed by the official geologist for Pennsylvania of the U.S. Geological Survey and also by Prof. Hallock, of Columbia University, New York, for drawing on the earth's internal heat by means of deep borings. The idea is to admit cold water into a deep boring and utilise the hot water and high-pressure steam produced. Mr. Hodges points out that he made similar suggestions in the *Popular Science News* for January, 1894, in an article on "Our Heat Resources of the Future". He remarked, however, at the time, "The great objection to this drawing on the earth's ancient store of thermal energy would be that her cooling and consequent shrinking would be accelerated; in other words, earthquakes would necessarily become more frequent, and possibly more violent and destructive in their effects."
From *Nature* 13 November 1902.

50 YEARS AGO

Temperature of the Interior of the Earth
Bullen has derived both the density and the compressibility of the earth as functions of depth, and has found that the bulk modulus k, which is the reciprocal of the compressibility, is a linear function of the pressure p: $k = k_0 + ap$. Ramsey has re-examined this relation from the point of view of the theory of solids, and his conclusions agree with those of Bullen, namely, that the linear relation is valid both in the core and in the mantle below 1,000 km. Ramsey, however, found that the constant k_0 had different values in the core and mantle, although the derivative $dk/dp = a$ was sensibly the same… It is now possible to make an estimate of the adiabatic temperature gradient throughout the earth… Taking T at 1,000 km. to be 3,600° K., values of T can be estimated at all greater depths. It is found that the temperature at the boundary of the core and mantle is 4,350° K. and at the centre of the earth is a little greater than 4,800° K. The increase throughout the core is thus only 500°. The results should be of considerable interest to Bullard's theory of the transfer of heat from the core.
From *Nature* 15 November 1952.