100 YEARS AGO

A copy of the *Peterborough Advertiser* of May 7 has been sent to us, containing the announcement that radium has been found in beds of Oxford Clay near Fletton, Huntingdonshire. No particulars are given, but a long descriptive article on the discovery suggests that it will make "brickfields better than gold mines." These sanguine anticipations will perhaps be tempered by the following extract from a paper by Prof. J. J. Thomson, read before the Cambridge Philosophical Society on February 15:— "Radium was found in garden soil from the laboratory garden, in the Cambridge gault, in gravel from a pit at Chesterton, in still greater quantities in sand from the sea-shore at Whitby, in the blue lias at Whitby, in powdered glass, in one specimen of flour, and in a specimen of precipitated silica."

ALSO

In the souring of milk the amount of lactic acid developed may reach 0.80 per cent. in three or four days when the milk solidifies. In view of Sir O. Lodge's suggestion (NATURE, October 1, 1903), I have made experiments comparing the rate of acidification, in two to three days, with and without the influence of radium rays… It therefore appears to me that under normal conditions radium rays have little or no effect on the functions of the lactic acid bacillus.

From *Nature* 19 May 1904.

50 YEARS AGO

Mr. A. R. Thomson, R. A., has completed a painting on astronomy to decorate a wall in the entrance hall of the Science Museum, London, near the well-known Foucault pendulum. Mr. Thomson was given *carte blanche* to depict the subject of 'Astronomy', and he has chosen as his main theme the invention and development of the telescope. On the left the small sons of Dutch spectacle-makers are playing with combinations of pairs of lenses… In the centre of the picture Galileo is using his telescope, ministered to by three rather bewildered ladies. On the right the distrust and suspicion of this early period is shown by figures of authority against a background of burning books. The whole picture is dominated by the great two-hundred-inch Hale telescope, and the sky behind is an animated representation of heavenly bodies among the figures of the constellations.

From *Nature* 22 May 1954.

mechanism. In the first paper[4], the authors present this discovery and discuss its implications for understanding genomic evolution. Their second paper[5] describes how they capitalized on these findings to make a modified L1 element that is more than 200 times as active as normal.

L1 and its relatives are termed retrotransposons because their transposition involves reverse transcription — the copying of RNA into DNA. Retrotransposition of L1 begins with transcription of the L1 genomic (DNA) sequence to form messenger RNA (mRNA) copies, a process carried out by a cellular enzyme called RNA polymerase (Fig. 1). The resulting RNAs serve both as templates for the production of L1 proteins (ORF1p and ORF2p) and as templates for retrotransposition. ORF1p binds and organizes the L1 RNAs, whereas ORF2p contains two enzymatic activities — the reverse transcriptase and an endonuclease.

The endonuclease makes a DNA nick in a target chromosome (Fig. 1). The reverse transcriptase then extends one of the freed DNA ends, using the L1 RNA sequences as a template, thereby making a single-stranded DNA copy of the L1 RNAs at the nicked site. Next, the new L1 DNA sequence becomes double-stranded and fully integrated through a series of, as yet ill-defined, further steps. As a result, a copy of the L1 sequence appears at a new location in the genome — often within a gene. The nicking reaction is weakly sequence-specific (it favours DNA that is rich in adenine and thymidine bases), but the target sequence is common enough for L1 elements to be able to hop into much of the human genome.

Nonetheless, the rate of L1 transposition today is very low. This is because the L1 RNAs and proteins accumulate only to very low levels in non-reproductive cells (the proteins are expressed more efficiently in germline cells, explaining why people often differ in the insertions in their genomes). In the first of the new papers, Han, Szak and Boeke[4] describe how they tracked this weak accumulation down to barriers within the L1 DNA sequence that prevent the efficient passage of RNA polymerase. They fused the ORF1 or ORF2 DNA sequence to marker genes, and showed that the hybrid mRNA accumulated much less than did the marker gene mRNA alone.

Curiously, this effect was independent of the orientation of the L1 DNA — but the mechanism varied. When the L1 sequence was in the same orientation as the marker gene, transcription began but elongation of the mRNA was inhibited. In the opposite orientation, the polyadenine — poly(A) — sequence that is characteristic of the tail end of mRNAs was added prematurely (a mechanism that has been suggested previously[6]).

Boeke and colleagues[4] also carried out a bioinformatics study of the human genome,

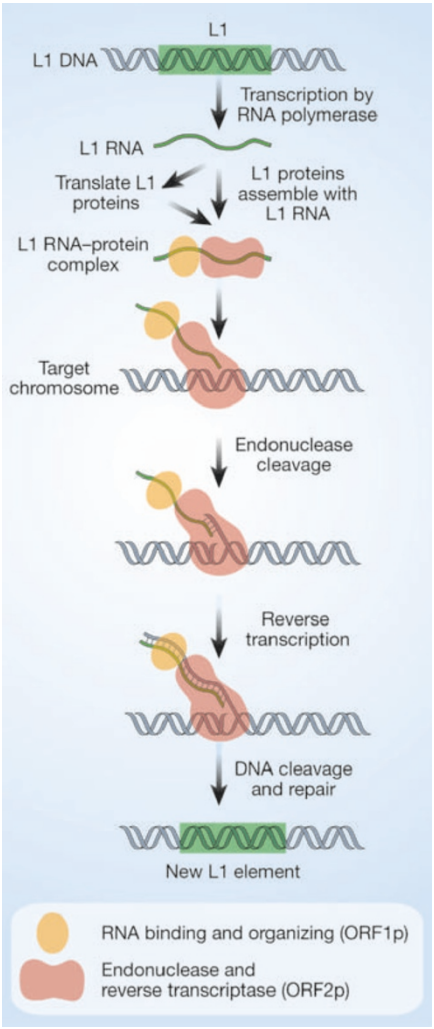

Figure 1 **Retrotransposition of the L1 element. The process begins when the DNA sequence encoding an L1 element is transcribed into RNA by RNA polymerase; the L1 proteins ORF1p and ORF2p are then made, using the RNA as a template, and the RNA and the proteins form a complex. The complex binds to another part of the genome and the endonuclease makes a nick in the DNA, generating a free end. The reverse transcriptase uses this free end as a 'primer', allowing it to start synthesizing a single-stranded DNA copy of the L1 RNA. The RNA is then removed (not shown) and the single-stranded DNA is used as a template to make double-stranded DNA, which is then seamlessly stitched into the nick in the chromosome. Thus, a new L1 element has been made in the genome.**

which revealed that these obstacles can be imposed on a cellular gene through the integration of L1 sequences. Specifically, the authors found that some 79% of human genes have L1 sequences in their non-protein-coding regions (introns) — and that high L1 density correlates with low levels of accumulation of the mRNAs encoded by these genes. These findings support a model in which L1 insertions in introns regulate cellular gene activity by diminishing the efficiency of mRNA elongation or promoting