100 YEARS AGO

The results obtained by culture under the influence of electric light are fairly well known, and the growing of lettuce for salads, in spacious greenhouses with the aid of electric light, is already a profitable industrial pursuit in the United States. However, the use of electric currents for stimulating vegetation, although it was studied more than fifty years ago, still remains unsettled. A communication upon this subject contains some welcome information upon the work done in this direction in Russia. … V. A. Tyurin ascertained that electrified seeds germinated more rapidly, and gave better fruit and better crops (from two and a half to six times higher) than seeds that had not been submitted to preliminary electrification. He also found that potatoes and roots grown in the electrified space gave crops three times heavier than those grown close by on a test plot; the carrots attained a size of from ten to twelve inches in diameter.

From *Nature* 19 April 1900.

50 YEARS AGO

During the centenary year of the death of William Wordsworth at Grasmere in Westmorland on April 23, 1850, slightly more than eighty years after his birth at Cockermouth in Cumberland, the poet's message and outlook upon life and Nature will be reviewed from many angles, and so it seems fitting that his work should be considered also in relation to scenic influences, especially from the regional or geographic point of view. This, indeed, is particularly called for in the case of one occupying a unique place in English literature as a mystical lover of Nature and identified with a most distinctive and beautiful part of England — the Lakes. Wordsworth's very position as the local interpreter of Lakeland is much enhanced by the fact he was yet no mere local figure. Apart from the universality of his theme, he travelled extensively over the British Isles and the Continent, so that a wide and varied geographical range is reflected in the poetry. Every one of his biographers has either stated or implied that to know Wordsworth is to understand the Lakes, and to understand the Lakes is to realize that this, on its own small scale, is a true mountain land — a fact which those who rush through the district in cars and never explore its inmost recesses can easily miss.

From *Nature* 22 April 1950.

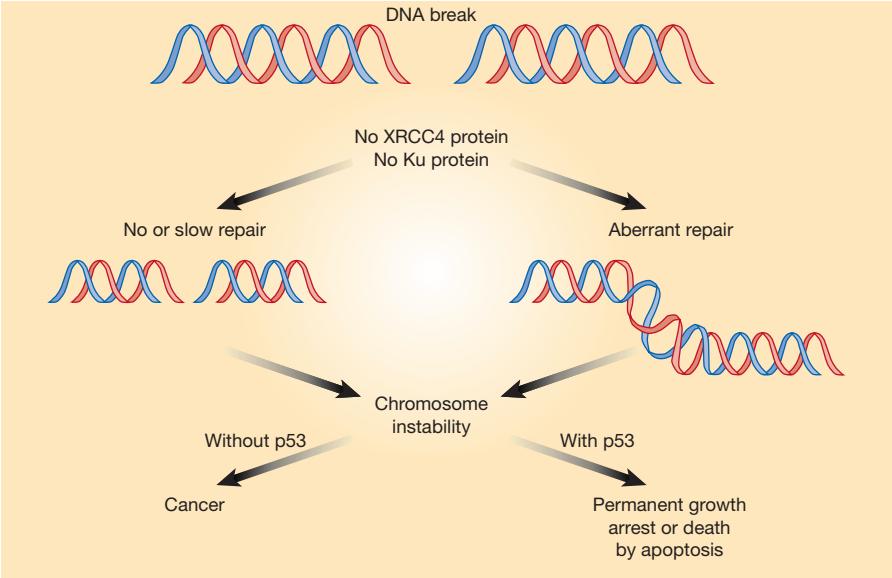

Figure 1 **Custodians of the genome. XRCC4 and Ku are 'non-homologous-end-joining' (NHEJ) proteins involved in repairing a particular type of DNA break. When cells lack one of these proteins, they fail to repair breaks correctly, or do so only slowly. This can lead to genomic instability and chromosome rearrangements. The tumour suppressor p53 may protect an organism against such potentially cancer-causing events by removing affected cells from the picture — either by causing them to die or by putting a permanent brake on their multiplication. In mice lacking either XRCC4 or Ku and p53, B-cell lymphomas develop within about three months after birth, as shown by Difilippantonio *et al.*[2] and Gao *et al.*[3]. These results firmly establish the NHEJ proteins as genomic 'caretakers', guarding against cancer.**

in that they bear specific chromosome translocations and gene amplifications involving the genes encoding the immunoglobulin heavy chain (IgH, an antigen receptor) and the c-Myc oncoprotein. The authors find break points near the so-called joining (*J*) segment of the IgH gene. Perhaps, deprived of their normal joining mechanisms, the broken ends created by the *V*(*D*)*J* recombination machinery contribute to oncogenic rearrangements, as seen in the p53- and DNA-PK-deficient mice[11]. This hypothesis could be tested by mating the doubly mutant animals with mice lacking the recombination-activating genes (RAGs). Theoretically, the triply mutant offspring of such crosses should not be able to generate broken DNA ends by *V*(*D*)*J* recombination (because they lack RAGs), so their inability to repair such broken ends (because they ack an NHEJ protein) should not lead to lymphomas. Indeed, this theory has been validated for mice lacking p53, DNA-PK and RAGs[11].

The presence of chromosome rearrangements and abnormal chromosome numbers in fibroblast cells derived from the double mutant mice[2,3] highlights the critical function of NHEJ proteins in maintaining genomic stability. Why do NHEJ mutations lead to instability? One might think that disabling the NHEJ pathway would simply lead to death of cells suffering the double-strand DNA breaks that NHEJ proteins usually mend. However, mammalian cells possess efficient alternative end-joining pathways that do not depend on XRCC4 or Ku[12]. These alternative pathways may be error-prone, and could lead to oncogenic chromosome rearrangements. p53 may normally offer protection against these events by removing cells with unrepaired (or slowly repaired) double-strand breaks from the picture, either by apoptosis or by a permanent block to the cell-division cycle (Fig. 1).

Indeed, cells from mice lacking Ku or XRCC4 exhibit senescence — permanent growth arrest — early on, and Ku-deficient mice show signs of premature ageing[7,9,13]. Removal of p53 rescues embryonic fibroblasts of both mutants from early senescence[2,3]. Premature senescence in the single mutant mice may result from a p53-dependent growth arrest in response to incorrectly repaired double-strand breaks (Fig. 1). Such breaks might result from oxidative damage, errors in DNA replication[14], or defective metabolism of chromosome ends (telomeres). Unfortunately, the early death of the mice as a result of lymphomas impedes assessment of the effects of p53 deficiency on premature ageing at the organism level.

On another note, the widespread apoptosis of developing neurons in mice lacking XRCC4 or DNA ligase IV (ref. 9) raised two questions. First, is the formation of double-strand breaks a normal feature of neural development? And second, do programmed gene rearrangements — analogous to *V*(*D*)*J* recombination in developing lymphocytes — occur during neuronal differentiation? It now appears that the answer to both of