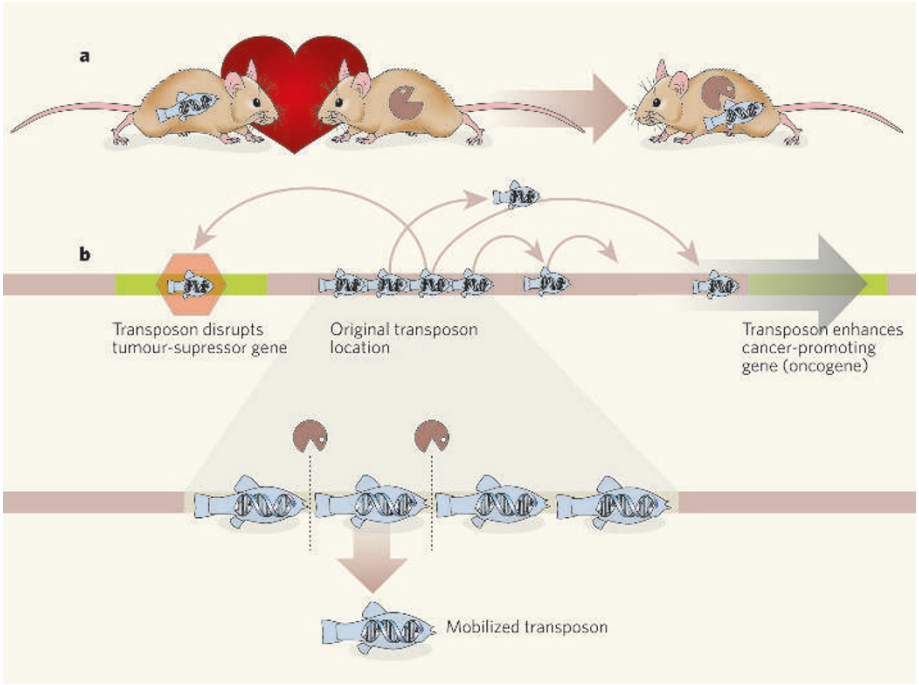

Figure 1 | DNA leaps out of fish and into cancer research. **a**, Mice whose cells contain many copies of the Sleeping Beauty transposon from fish are bred with mice whose cells make the SB transposase at high levels. Cells in the offspring contain both the transposon and transposase (pacman), allowing the transposon to hop about the genome. **b**, The transposase binds to and excises the transposon from its starting location in the genome. The excised transposon can reintegrate elsewhere in the genome, sometimes near to or within a cancer-related gene. If the transposon inserts in a gene, it will truncate the encoded protein, usually destroying its function. This will identify genes that help to protect against cancer (tumour-suppressor genes). Inserting near a gene causes an increase in gene product. This will identify cancer-promoting genes (oncogenes).

identify cancer genes, imagine the genome as a book of instructions on how cells work. SB is like a small phrase or set of directions that can hop into, and potentially alter, any instruction in the book. Sometimes, inserting the phrase will cause insignificant changes, but if SB alters instructions for key processes, such as cell proliferation or cell death, the cells can grow and divide beyond their normal potential and become cancerous. The authors designed the SB transposon to disrupt gene function in two ways. If it inserts in a gene, it will truncate the protein encoded by that gene, usually destroying its function. This will identify genes that help to protect against cancer (tumour-suppressor genes). If the transposon inserts near a gene, it causes an increase in the gene product, allowing cancer-promoting genes (oncogenes) to be identified.

By isolating the sites of SB insertion in tumours, the groups tagged genes that are known to be important in the development of cancer and those likely to be involved in the disease that had not previously been associated with it. Dupuy *et al.*[3] also demonstrated networks of genes that interact to cause cancer. In addition, Collier *et al.*[4] show, using animals that harbour cancer-predisposing mutations, that the SB system can tag genes in a solid tumour called a sarcoma. This tumour can involve various tissue types, including neural cells and connective tissue cells.

Cancer is rarely caused by the mutation of a single gene; rather, perturbations of several genes tend to cooperate to cause the disease[6]. Genetic pathways involved in the development of leukaemia have been dissected by tagging with mouse leukaemia retroviruses[7,8], but gene networks in other tumour types are less well studied. The development of new treatment strategies would ideally require information on all the genes involved in common and devastating cancers such as breast, colon, prostate and lung cancer, and the SB system seems a promising way to provide this.

The technology is likely to be very powerful, because the transposase can be designed to be expressed selectively in a specific cell type or developmental stage, so that transposition will occur only in those cells or at that time. Many cancer-associated genes are disrupted in only one particular cancer, and the selective SB technique can be used to locate these. Furthermore, the ability to limit transposase expression will enable the system to be turned on to make mutations and then turned off to stabilize them. It also allows for the controlled excision of the transposons, so that mutations can be reversed.

At present, however, the ability to restrict gene expression to each type of tissue-specific stem cell is limited[9]. (Tissue-specific stem cells are the immature cells that give rise to specialized tissues, where cancer mutations are most likely to occur.) Further research into stem-cell-restricted gene expression

50 YEARS AGO

Another milestone was reached in the history of the European Organization for Nuclear Research, when on June 10 the foundation-stone was laid of the laboratories at the Meyrin headquarters of the Organization near Geneva, followed by the signature of an important Agreement between the Organization and the Swiss Government... Those who have been closely associated with the years of planning came away feeling that this unique Organization has good reason to be proud of what has been achieved so far. The high level of scientific and technical competence of the research and design teams and the spirit of enthusiasm which animates all concerned provide solid grounds for confidence in the healthy growth of the new Organization.
From *Nature* 16 July 1955.

100 YEARS AGO

"The popularisation of science." *The New Knowledge* by Robert Kennedy Duncan.
The author of this attempt to make the progress of recent discovery in chemistry and physics understanded of the people remarks in his preface:— "The great expositors are dead, Huxley and Tyndall and all the others; and the great expositor of the future, the interpreter of knowledge to the people, has yet to be born." And (but it must be added quite modestly) he attempts to wear the cloak of prophet... To give the reader an idea of the author's style, a quotation from the first paragraphs of part ii may be made... "Here, for example, is a swarm of atoms, vibrating, scintillant, martial,— they call it a soldier,— and, anon, some thousands of miles away upon the South African veldt, that swarm dissolves,— dissolves, forsooth, because of another little swarm,— they call it lead."... Now this purports to be very fine writing, but does it gild the pill of science? I am inclined to think not. Still, tastes may differ.
From *Nature* 13 July 1905.

50 & 100 YEARS AGO