

lines of mice, adenocarcinomas of mammary origin appeared in multiparous females at the time of pregnancy. The hormonal induction of expression that occurs in the lactating mammary gland is presumably prerequisite for the accumulation of sufficient levels of the *c-myc* oncogene product to induce the first step of tumorigenesis.

Although the *in vitro* experiments that suggest the existence of at least two classes of oncogene required for the transformation of primary cells¹¹⁻²⁰ have aroused much interest, it is important to extend these findings to *in vivo* studies. Hanahan's results show that SV40 large-T antigen induces proliferation of the β -cells and the subsequent hyperplasia but suggest strongly that this is not sufficient to induce a tumour, otherwise all the hyperplastic islets would progress to tumours¹⁰. Similarly, tumours arise in only a few of the mammary glands of the mice carrying mammary tumour virus/*c-myc* oncogene. In these situations some second event must be required for tumorigenesis. An *in vivo* system in which the multi-step nature of tumorigenesis can be analysed has thus been established.

In vitro experiments are severely limited by the availability of suitable lines of cultured cells and by transfection efficiencies, whereas *in vivo* experiments allow expression of the oncogene to be targeted to any cell type for which an appropriate transcriptional control sequence is available. Large-T antigen could thus be expressed in many different cell types to ask whether the second event always affects the same gene or whether there is cell-type specificity for the subsequent event(s). Conversely, the insulin upstream region could be used to target the expression of other oncogenes to the β -cells to ask, first, whether hyperplasia and subsequent tumorigenesis are induced and, second, whether the subsequent event(s) is general, or specific to the initiating oncogene. Finally, two or more oncogenes could be targeted simultaneously to the same cell type. Such studies will greatly advance our understanding of the multi-step nature of oncogenesis. Equally important, they will enable molecular studies on tumour types for which there is no good *in vitro* model. The system should also make possible the study of processes, such as angiogenesis, metastasis and immune surveillance, that are hard to study *in vitro*.

It is curious that the β -cell tumours seem not to induce an immune response. SV40 itself is an extremely weak carcinogen in mice; tumours arise very rarely and with a long latent period^{21,22}, presumably because the small proportion of the large-T antigen that is displayed on the surface elicits a powerful immune response.

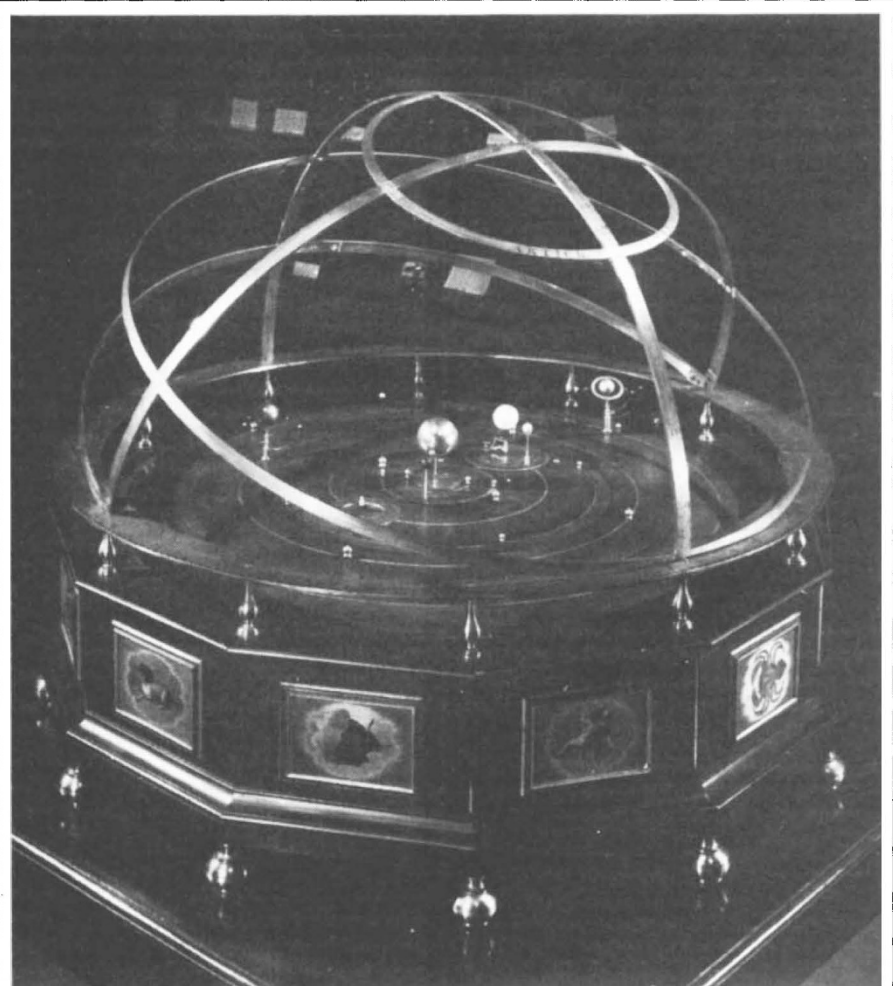
The severe disorganization of the other cell types in the endocrine pancreas induced by β -cell proliferation and hyperplasia is also of interest. The ability to perturb the growth of one cell type in complex

interacting system will allow studies of the mechanisms that normally control the orderly growth and behaviour of an organ.

One further use of this type of study derives from the ability of many oncogenes, including those discussed here, to 'immortalize' cells. Thus, it may be possible to establish cell lines derived from all tissues of mice carrying such genes in their germ line. Indeed, it has already been shown that cells can be readily grown from a number of the tissues of the SV40 transgenic mice (A.J. Levine, personal communication). Such lines have considerable practical use. Commercial manufacture of some proteins may be limited by the inability of commonly used cell types to perform some post-translational modifications. The problem would be overcome if established lines of cells normally making the protein were available. □

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Celestial mechanics

THIS fine example of an orrery, or mechanical model of the Solar System, is one of the early scientific instruments on display in the exhibition "Science and Profit in Eighteenth Century London" at the Whipple Museum of the History of Science in Cambridge until 6th December 1985. Orreries, used to teach the astronomy of the Solar System, were not made to scale but illustrate the relative positions and motions of the planets and their moons. This one, made by Geo Adams at Tycho Brahe's Head in Fleet Street, London, is calibrated for the Julian calendar, which dates it before 1752. It includes Saturn with its rings and the five moons found between 1655 and 1684, but not Uranus, which was discovered only in 1781. Other instruments in the exhibition include an altazimuth theodolite, made about 1740, a compound microscope improved by tilting the limb for extra comfort, and a reflecting telescope.