organising centres (for example the centriole and, probably, its associated material) seem to be diverted from alternative activities in preparation for mitosis at about the time that DNA replication is initiated. This is reminiscent of the sequence of events which occurs in the division cycle of the yeast *Saccharomyces cerevisiae* (Hartwell *Bact. Rev.* **38**, 164; 1974) where mutation of the gene controlling the replication of the spindle pole body (a microtubule-organising centre analogous to the centriolar complex) blocks the initiation of DNA synthesis and hence of other steps leading to mitosis. The timing of centriole duplication in mammalian cells is not yet determined, but may occur in late G_1 or early S (see also Rattner & Phillips *J. Cell Biol.* **57**, 359; 1973).

Although a useful marker for some cells, primary cilia are absent from others and it should not be forgotten that higher plant cells may not possess centrioles (see *News and Views* **277**, 515; 1979). Higher plants do, however, possess amorphous microtubule-organising centres analogous to the amorphous type which surrounds the centriole in animal cells and plays a more direct part in forming the mitotic apparatus. Telzer and Rosenbaum (*J. Cell Biol.* **81**, 484; 1979) have isolated such pericentriolar material from HeLa cells and demonstrate that when isolated from mitotic cells it supports reassembly of microtubule protein into microtubules, but is ineffective when obtained from cells in interphase. Considered together, recent evidence points to a close association between the activity of microtubule-organising centres (both structured and amorphous) and the mitotic cycle. In view of this it may be useful to consider even the cells of multicellular organisms as 'differentiated flagellates' which undergo a metamorphosis to the reproductive stage driven by signals affecting microtubule organising centres. □

Immunotherapeutic T cells?

from Peter Beverley

TWENTY years ago Thomas proposed the theory of immune surveillance. Since then it has been a hope of cancer immunologists that the immune system might be persuaded to do the work of physicians and surgeons and destroy the tumours of cancer patients.

Initially, because of their role in allograft rejection, thymus-derived lymphocytes (T cells) were thought to be the main agent of surveillance. Later data have thrown up other candidates for the role of 'surveyor' (Baldwin *Nature* **270**, 557; 1977) and the very idea of surveillance has been challenged (Moller & Moller *J. Natn. Cancer Inst.* **55**, 755; 1975). Nevertheless T cells remain an attractive possibility for immunotherapy because of their extreme specificity of response and because high levels of activity can be generated by stimulation *in vitro*.

The practicality of immunotherapy rests on a number of assumptions. First that tumours carry surface antigens distinct from those of normal cells; second that lymphoid cells of the tumour-bearing host can be immunised against the tumour antigens; and third that immune cells (or antibodies) when administered to the tumour-bearing animal will be effective in reaching and destroying the tumour.

Experimental tumours often provoke an immune response, but in many cases it has been shown that immunity is directed against antigens coded by RNA tumour viruses carried in the tumour cells, while in general the evidence for immunogenic antigens on spontaneous tumours of animals is far weaker. In man apparently, tumour-associated antigens have been defined using heteroantisera but it is not clear whether these antigens provoke a T cell response by the tumour bearer. Similarly, although there have been many reports of cell-mediated immune responses to tumours in man, their exact nature and specificity have been difficult to define because the responses are weak and inconstant. Thus the two findings that T cells cytotoxic for human leukaemias could be generated (Sondel *et al. J. Immun.* **117**, 2197; 1976) and that specific cytotoxic cells could be propagated indefinitely *in vitro* (Gillis & Smith *Nature* **268**, 154; 1977) raised the hope that some of these problems might be resolved by the production of large numbers of highly active cytotoxic T cells directed at human tumour antigens.

This has now been achieved by Joyce Zarling and Fritz Bach, (this issue of *Nature*, page 685) and the power of the new methodology is certainly demonstrated. Previously, not all leukaemia patients could be shown to respond to their own leukaemia cells (Lee & Oliver *J. exp. Med.* **147**, 1334; 1978) but a combination of stimulation *in vitro* followed by expansion of the cytotoxic T cell population *in vitro* (up to 10 million-fold) reveals that virtually all patients can make an immune response to their own leukaemia cells. Furthermore, since stimulation with a pool of allogeneic lymphocytes was effective in generating kill against autologous leukaemia cells, it may be possible to generate cytotoxicity against a tumour even if no tumour material is available (important for immunotherapy of solid tumours where stimulator cells may be hard to obtain). That pooled allogeneic cells are effective reinforces the immunologists' dogma that transplantation antigens (HLA) in some way determine or are related to the T cell repertoire.

On the face of it the finding that T cells can be sensitised to autologous leukaemia cells and that other cells are not killed would seem to be strong evidence for tumour-specific antigens on leukaemia cells. However, this is a conclusion which should be regarded with considerable suspicion. Recent studies of leukaemia cells from many laboratories suggest that at least the majority of leukaemias have surface membrane phenotypes characteristic of normal, though sometimes rare, cells. A cautionary tale is provided by the acute lymphoblastic leukaemia (ALL) antigen which, although first discovered on leukaemia cells and thought to be ALL specific is in fact found on bone marrow stem cells in fetal and regenerating bone marrow (Greaves & Janossy *Biochim. biophys. Acta* **516**, 193; 1978). As yet no controls carried out in studies of autologous anti-leukaemia cytotoxic T cells have proved that the target antigen(s) for the killer cells are not just the same sort of normal differentiation antigen. If immunotherapy involved elimination of a stem cell population along with the leukaemic cells it might not be so attractive a proposition!

Delivery of immunotherapy is an additional problem. In animal experiments immunised cells have been most effective when administered mixed with tumour cells in local tumour growth assays. The relative inefficiency of systemically administered cells may be due either to incorrect migration *in vivo* of cultured lymphocytes or because more than one subset of lymphocytes is required for optimal elimination of tumour cells.

Even if there remain doubts about the use of T cells amplified *in vitro* for therapy, there can be no doubt that cultured T cells will be extremely useful tools. Not the least important of the questions which will surely soon be answered, doubtless using cloned sublines of killers, is what is the nature of human leukaemia antigens? If they turn out to be exclusively tumour-associated, the way to T cell immunotherapy may be open. □

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