arylsulphatase B activity persisted for the length of the study, 250 days. The most objective sign of clinical improvement was a resolution of corneal clouding, although other signs, such as the cat's ability to walk and chew, its coarse facies and demeanor, also seemed to improve. It will be of interest to determine how much clinical improvement is possible in this and similarly-treated cats, and to document the pathological improvement at the end of their substantially lengthened lives.

Animal models for inborn errors of metabolism could lead the way to a much wider use of clinical marrow transplantation. Animals will be particularly valuable for testing methods of broaching or circumventing the blood–brain barrier in those conditions with neurological sequelae[12]. □

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Immunology

T-cell receptor companions

from M. J. Owen

WITH the molecular analysis of the T-cell antigen receptor, molecular biologists have recently begun to solve the outstanding immunological question of how T cells recognize antigens and thus contribute towards the antigen-specific immune response. As already described in these columns[1], the receptor is composed of a β chain, which was well defined some months ago, and an α chain whose partial amino acid sequence[2,3] has recently confirmed a tentative indentification from cDNA clones[4,5]. But the heterodimer formed by these two chains can, so far as is known, subserve only the recognition function of the molecule. Some other structure, therefore, must be responsible for transducing the signal to the interior of the cell and initiating the cellular response to antigen. An obvious candidate for this function is the so-called T3 molecule, which is physically associated with the receptor heterodimer[6]. T3 is a glycoprotein complex of three polypeptide chains (γ, δ and ξ). It, too, is beginning to yield to the all-embracing techniques of molecular biology as shown, in particular, by a paper from Terhost's laboratory on page 413 of this issue[7].

The T3 glycoprotein is unlikely to play a direct role in specific binding of antigen but is nonetheless probably obligatory for receptor function and may play a part in the stabilization of the initial interaction between receptor and antigens, as well as in signal transduction[8]. In this regard it is intriguing that calcium fluxes can be induced in T cells by antibodies against the T3 glycoprotein[9]. Furthermore, the expression of T3 is apparently linked to that of the antigen receptor, since in no case has one been detected at the T-cell surface in the absence of the other.

To clone the δ chain of T3, Terhorst's group has used the protein sequence route in which oligonucleotide primers are synthesized on the basis of a partial protein sequence and used as probes with which to extract the desired cDNA species. (It is worth pointing out for the afficionados that the hybridisation probe used was a 19-mer and 15-mer mixture, consisting of 576 and 128 different sequences, respectively; this must represent a record for the redundancy of a primer used successfully in a cDNA cloning exercise.) The deduced primary sequence of the T3 δ chain confirms much of the biochemical data reported by Terhorst's group and by others, and contains few revelations or surprises. Predictably, it shows no sequence homology with members of the multi-gene family that includes the genes for the T-cell receptor, immunoglobulins and the major histocompatibility antigens. One point of interest is that the human δ-chain probe cross-hybridizes with a mRNA species in mouse T cells (as detected by Northern blotting analysis), which represents the first convincing demonstration of a murine equivalent of at least part of the T3 complex. The failure to identify a T3-like molecule on the surface of mouse T cells by means of serology has been a point of some concern to those who advocated a pivotal role for T3 in the T-cell response to antigen.

One possible clue to the mechanism of association of the α-β dimer with the T3 complex has emerged from this study. Tehorst's group point out that the transmembrane segments of the α and β chains of the structure both contain a lysine residue whereas an aspartic acid side chain is located in the corresponding region of the δ-chain transbilayer peptide. The ion pair that would form between these residues in the hydrophobic environment of the lipid bilayer would provide a strong stabilizing force for the T3–receptor complex. If this speculation is correct, *in vitro* mutagenesis experiments in which the transmembrane charged residues are altered should prove rewarding.

The minimal array of proteins involved in the response to antigen on the surface of an effector T cell seems to be the T3-receptor complex, the T4 or T8 glycoproteins, and possibly the mysterious protein described by Tonegawa's group and originally thought to be an α chain candidate[10]. The availability of clones encoding all of these surface structures will be necessary before molecular immunologists can begin to manipulate the system and provide a complete molecular description of the recognition and activation processes. The isolation of a cDNA clone encoding the δ chain is an essential first step towards defining the role of T3. The partial protein sequence of the T3 ξ chain reported on page 455 of this issue[11] should provide the basis for the cloning of its cDNA. And the deduced protein sequence of this chain will prove especially interesting since it is postulated by Terhorst and his colleagues to be a constituent of a putative calcium channel involved in the process of activation of the T cell. At the current rate of progress, it should not be long before the sequence is reported and can be commented on in these columns. □

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100 years ago

OVER-PRESSURE IN ELEMENTARY SCHOOLS

Take the typical case of a class of seventy children, starting with about the same attainments. The bulk of these will be average boys, or girls, as the case may be, fairly healthy and intelligent, not given to over-much study, but still ready to fall in with the requirements of the school. But there will also be some half-starved children who often come without any breakfast, dull children — descendants of a wholly uncultured race — feeble children, and others averse to any restraint and constitutionally irritable, together with children who are weary with toil at home. Besides these there are the exceptionally clever children, who are in danger of under-pressure and the over-sensitive or ambitious who are prone to overwork themselves. It is evident that the general scope of the instruction must be adapted to the average of the class.

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