work theory — that idiotypes shared between T and B cells result from a shared genetic pool of *V* segments for B- and T-cell receptors for antigen — has already been excluded by molecular biology. How the cloning of the receptor genes has advanced the understanding of the T-cell receptor repertoire was the other main topic of the meeting.

T-cell receptor

Unlike B cells, T cells are able to respond to antigen only when it is presented to them in association with a cell-surface protein, a product of the major histocompatibility complex (MHC) of the animal in question, a phenomenon called MHC restriction. There has been much debate concerning whether such a feat requires one receptor or two, the bulk of the evidence strongly suggesting that a single T-cell receptor, made up of an α/β heterodimer, is sufficient (see Robertson, M. *Nature News and Views* **317,** 768; 1985). M. Steinmetz (Basel) presented further evidence from transfection experiments to support this point of view (Dembic, Z. *et al. Nature* **320,** 232; 1986). He and his collaborators have used α- and β-chain genes from a cytotoxic T cell specific for the hapten, fluorescein (FL) in association with the MHC product D^d, to transfect a T cell specific for a different hapten and MHC product and with this transferred the specificity for FL/D^d of the donor. This supports the earlier evidence that no clone-specific, variable molecule besides α and β contributes to the specificity of these cells.

The precise contribution of the α- and β-chains to the recognition of MHC and antigen, however, remains unclear. Several investigators reported the results of sequencing α- and β-chain genes from collections of T cells with related specificities for antigen and MHC, in the hope of discovering some correlation between the sequences and the specificities. S. Hedrick (University of California at San Diego) and A. Winoto (California Institute of Technology), for example, had used T-cell clones specific for a pigeon cytochrome C peptide, and with well-defined MHC reactivities (Fink, P.J., Matis, L.A., McElligott, D.C., Bookman, M. & Hedrick, S.M. *Nature* in the press). But although there were suggestions of some correlation between antigen specificity and a region of the β chain around the diversity (D) region (Fink, P.J. *et al.* and Winoto, A.), or the J region (A. Iwamoto, Toronto), J_β regions may also contact MHC (Iwamoto; K. Eichmann, Freiburg), so no general rules are yet apparent.

Gamma revisited

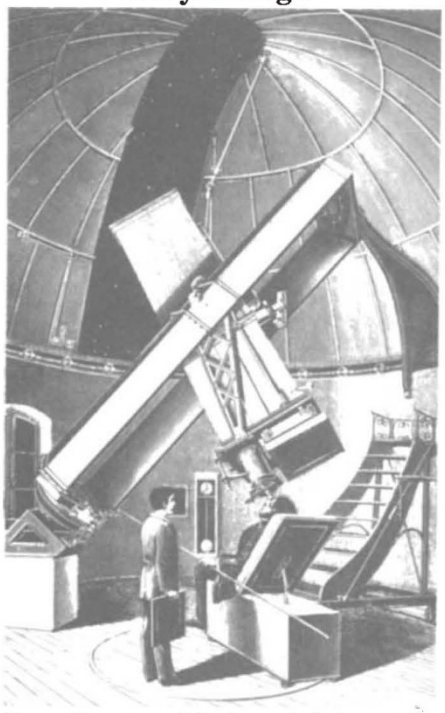
Such experiments still leave unresolved one of the major current T-cell mysteries; the problem of the role of γ chains. About eighteen months ago, Susumu Tonegawa and his colleagues at MIT reported the existence of a T-cell receptor-like complementary (c) DNA clone, the genes for which rearrange and are expressed only in T cells. Because the sequence and glycosylation patterns of the polypeptide predicted from the cDNA sequence did not match known α- or β-chain properties, the predicted protein has been named γ; it has yet to be identified as an entity. Much is known from cDNA and genomic sequences, however. Gamma products, which were at first though to be relatively invariant, are becoming more variable: T. Mak (University of Toronto) and D. Raulet (MIT) respectively, described a new constant (*C*) region and three new *V*-region genes in this complex, bringing the total number of known γ-chain genes in most mouse strains to four *C* regions (three of which cross-hybridize), each with a *J*, and six *V* regions (three of which cross-hybridize with each other). As in the mouse immunoglobulin λ locus, each *V* seems to rearrange to a particular *J*–*C* pair. Some *V* and *J* segments seem to be intrinsically non-functional.

The additional variability in the gene family implies that the product may play some part in specific recognition, and it has been suggested that it is essential for the function of mature cytotoxic T cells, the cells with which it was originally associated by Tonegawa, because of higher messenger (m) RNA expression in these cells than in helper-T cells. This possibility seems to be excluded, however, not only by the experiment of Steinmetz's group, but also because most rearranged γ-chain genes in peripheral T cells are non-functional, often because they contain termination codons consequent on out-of-frame joining of *V* to *J* regions. E. Reilly, from H. Eisen's group at MIT (Reilly, E.B. *et al. Nature* in the press), for example, has sequenced 11 different cDNA clones from three cytotoxic T-cell clones and found all to be non-functional, and similar examples are available from other laboratories.

The more recently discovered non-cross-hybridizing C_γ genes and the three new non-cross-hybridizing V_γ genes leave open the possibility that the functional γ-chain cDNA in these peripheral T cells has yet to be sequenced. Alternatively, functionally rearranged γ-chain genes may be present at an early stage in the history of the T cell and be lost before maturity. In support of this notion, Raulet (MIT) showed that rearrangement and mRNA involving two particular γ-chain *V* regions gradually disappear from thymocytes and peripheral T cells as the animal ages. He suggested that these *V* regions lie downstream (3′) of a third *V* region. A functional rearrangement to one of the 3′ regions could be deleted during maturation by the subsequent rearrangement of an upstream *V* by a mechanism similar to that described above for V_H genes.

If γ chains do play a part at a particular stage in the life of T cells, when is this likely to be? The γ mRNA is expressed at high levels in early fetal thymocytes illustrated at this meeting by the work of R. Snodgrass (Basel) and D. Pardoll (National Institutes of Health, NIH). It is not clear that these high levels of mRNA imply that there will be high levels of protein, however, because γ-chain rearrangements are rare in hybridomas prepared from early fetal thymocytes (W. Born, Denver) and not universal in adult 'early' thymocytes (M. Davis, Stanford University). Moreover, much of the fetal thymocyte mRNA, as in mature T cells, turns out on sequencing to contain frameshifts making it non-functional (Snodgrass). The cDNA may be overrepresented in non-functional transcripts, as Raulet reported that five out of six rearranged genomic DNA γ clones prepared from day 17 mouse fetal thymuses turned out to have open reading frames. The implications of all this, that γ proteins may be used only in small numbers for a short time during thymocyte development, and that the protein may down-regulate gene expression, are very intriguing in the light

100 years ago



Some attempts made last year at photographing the heavens by means of an instrument quite rudimentary having yielded good results, the director of the Paris Observatory gave orders for the construction of a special apparatus, the design of which is shown in the figure. This new instrument is composed of two telescopes in juxtaposition inclosed in a single metallic tube in the form of a parallelopiped, and separated from each other along their whole length by a narrow partition.

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