

precursor) responses; whereas IgG1 antibodies stimulated anti-streptococci B clones (at high concentrations) or both B and T anti-streptococci clones (at low concentrations).

These two sets of observations strongly suggest that T cell clones have on their surface a molecular structure—presumably the antigen receptor—which bears idiotypic antigenicity similar if not identical to that of B cell receptors and B cell-derived serum antibodies. Although unequivocal evidence for the biosynthesis of this determinant by T cells is not yet available these results clearly imply that T and B lymphocytes are equipped with a similar 'immunoglobulin' *V* gene pool and may have at least some identical genes.

Presumably the amino-terminal end of the T cell receptor polypeptide contains both the idiotypic determinant and the antigen combining site. The crucial question now is the nature of the remainder of the molecule. Is it an *Ir* region gene product with invariant peptide sequences and domains analogous to those coded by immunoglobulin C (constant) genes? If this is the case and *V* genes are identical in T and B cells we have the problem of how unlinked *V* and *C* (*I* region) gene products become associated, since in B cells the gene pairs are linked and association is believed to occur at the transcriptional level. Alternatively, could the T cell receptor have an immunoglobulin (of a new class?) *C* region after all? J. Marchalonis and N. Warner suggested that this latter view was strongly supported by their evidence that almost all T-cell derived neoplasms synthesise immunoglobulins. Significantly, with respect to other discriminating lymphocyte cell surface products (for example  $\theta$ , Ly antigens) these lymphomas maintain a strict T cell phenotype.

The former view is however probably the popular choice and presumably immunochemical analysis of the Wigzell-Binz idiotypically defined T cell product should soon resolve the issue. This interpretation is also supported indirectly by an elegant series of experiments by M. Taussig and A. Munro (see this issue of *Nature*, page 103). Their important and provocative results suggested that activated T cells released an *I* region coded glycoprotein (molecular weight about 50,000) which facilitates the B cell antibody response. The 'factor' probably has antigen specificity although this critical point has not been clearly established. Mice of different strains which did not respond to (T,G)-A-L may be deficient in T cells producing the factor, in B cells capable of 'receiving' the factor, or both! An observation of paramount importance was the result of crossing

T cell 'deficient' mice with B cell deficient mice; the  $F_1$  offspring were responders presumably by complementation of T and B cell *I* region-controlled immunocompetence.

A similar *Ir* gene complementation effect was reported by B. Benacerraf (Harvard Medical School) and was in fact reported with minimal effect by E. Rude and E. Gunther at the Second International Congress of Immunology last year (*Progress in Immunology II*, vol. 2, 223; Associated Scientific, 1974). The main conclusion emerging from the work of Taussig and Munro is that the *Ir* region may contain structural genes coding for cell surface glycoproteins (with Ia antigenicity) on both T and B cells. These structures are critically involved in antigen recognition and collaborative interactions between T cells, B cells and possibly macrophages as well. If this is correct then the *I* region contains genes which not only code for antigen binding sites but also for a 'mutual' recognition system (that is, of T cell Ia molecules by B cell surface Ia molecules).

It seems reasonable to suppose that the molecule studied by Taussig and Munro might be the same as the idio-type-bearing structure identified by Wigzell and Binz, although H. McDevitt (Stanford University) reported that anti-Ia sera could not block (T,G)-A-L antigen binding by T (or B) lymphocytes. Taken together however these results certainly created the strong impression that the T cell receptor mystery may be soon solved. In the meantime, some healthy scepticism is probably called for. T cell populations are clearly very heterogeneous and different types of receptors might exist on subsets programmed for distinct functions. The role of macrophage surface structures in the genetic control of T+B responses merits further consideration. The precise antigen specificity and diversity of putative T cell receptors requires clearer definition as do both their immunochemistry and the cellular site of biosynthesis and uptake.



### A hundred years ago

In connection with the calamitous floods around Toulouse, on the 25th June a singular phenomenon was observed at Clermont-sur-Lanquet. The whole of the earth on the slope of a mountain was moved bodily, a shepherd's house being transported uninjured to a distance.

from *Nature*, 12, 220; July 15, 1875.

## Calcium transport in contraction and secretion

from N. M. Green

The growing interest in the role of  $Ca^{2+}$  in a variety of intracellular control mechanisms was reflected in an international symposium on  $Ca^{2+}$  transport (Bressanone, May 10–16, 1975) which was devoted to establishing contact between workers in the field of muscular contraction, where the effects of  $Ca^{2+}$  are relatively well understood, with those who work on a variety of secretory systems. This report considers only a few of the fifty papers that were presented, emphasising those aspects which may lead to fruitful interactions.

ONE of the main technical problems in the way of a more precise definition of the role of  $Ca^{2+}$  in secretory systems is the difficulty of measuring changes in submicromolar, cytoplasmic  $Ca^{2+}$  concentrations in the presence of intracellular and extracellular reservoirs where concentrations are increased a thousand-fold. J. Meldolesi (University of Milan) described the analyses of subcellular fractions from pancreas. Interpretation was difficult because of the rapid exchange of  $Ca^{2+}$  between compartments after cellular disruption. However, there was an interesting observation of a large non-exchanging reservoir of  $Ca^{2+}$  in the zymogen granule fraction. A similar high  $Ca^{2+}$  content of secretory granules was observed in pancreatic islet tissue (W. J. Malaisse, University of Brussels) and in parotid gland (Z. Selinger, Hebrew University, Jerusalem). J. L. Borowitz (Purdue University) suggested that uptake of  $Ca^{2+}$  by the granules in adrenal medulla might play an auxiliary role in the post-secretory recovery process. A promising new approach to the problem of intracellular  $Ca^{2+}$  distribution is that of X-ray microprobe analysis which can detect changes of local concentrations of  $Ca^{2+}$  within organelles at a resolution of 50–100 nm, provided that local concentrations, which can be enhanced by microincineration, are high enough (T. A. Hall, Cambridge). A study (with R. Yarom, Hebrew University, Jerusalem) of cardiac muscle revealed unexpectedly high levels in cell nuclei, associated particularly with heterochromatin, suggesting that serious consideration should be given to the nucleus as a reservoir of intracellular  $Ca^{2+}$ . M. J. Berridge (University of Cambridge) described another application of the technique to show that