news and views

Antibody production made easier

from K. I. Welsh

THE latest paper from the laboratory of César Milstein (this issue of *Nature* page 550) reporting the construction by cell fusion techniques of a line of hybrid cells secreting antibody against rat major histocompatibility antigens, promises to be an important step forward in tackling some of the many clinical and biological problems concerned with the histocompatibility system which require a reliable and standard supply of anti-histocompatibility antigen antibodies for their solution.

Tissue matching for skin, cornea, bone marrow and kidney transplants depends to a large extent on stocks of reasonable titre monospecific typing antibodies against the major histocompatibility antigens. These precious sera, obtained from immunised volunteers, multiparous women, transplant recipients or primates take months or even years of laborious work to produce, test and become accepted as standard reagents. Antibodies, over 200 in all, are tested for lysis of recipient cells and potential donor cells; identical reaction patterns indicate identical recipient and donor histocompatibility type at the HLA-A, B, C and D locus. Commercial reagents are expensive, yet the use of antisera against histocompatibility products in the analysis of the association of particular diseases with the major histocompatibility complex (MHC) as well as for routine tissue matching, is increasing daily. The ideal solution to these serological problems would be for sufficient supplies of standard typing reagents to be available worldwide.

The isolation and characterisation of MHC products on a large scale and experiments designed to answer many basic questions related to the understanding of their evolutionary significance, present role and importance in tissue rejection and prevention of disease would also be made much easier

with a readily available supply of standard monoclonal antibodies to the MHC antigens.

Milstein *et al.* constructed their histocompatibility antibody secreting cell line by fusing a mouse myeloma cell line with spleen cells of AO-strain rats previously immunised against DA strain antigens. Clones grown up from individual hybridisations were tested for their ability to produce anti-DA antibodies, and a clone was selected which was further characterised as producing antibody against an individual K/D specificity of the Ag-B4 haplotype, thereby identifying the first uniquely defined antigenic specificity in the rat MHC. The authors hope that characterisation of the products of other clones will lead to the identification of other specificities of the Ag-B4 haplotype.

This work illustrates the latest use of basic techniques developed in Milstein's laboratory for producing hybrid cell lines secreting antibody of defined specificity (see Köhler & Milstein *Nature* 256, 495; 1975), a technique now being exploited in other laboratories.

At a recent discussion meeting at Cambridge K. Rajewsky and G. Hämerling reported that they have hybridised tumour cells with a variety of antibody-producing cells to obtain lines of cells synthesising antibody against a wide range of idiotypes as well as bacterial and mammalian cell components.

Antibody production from tissue cultures of such cells requires culture facilities on a larger scale than many laboratories possess. Rajewsky *et al.* have however developed an *in vivo* culture system which brings production of experimental quantities of antibodies from hybrid cells easily within the capabilities of most laboratories. The hybrid cells are injected into a histocompatible animal where they pro-

liferate, producing high levels of antibody which can be recovered from the animal's serum. This provides a method of obtaining experimental quantities of antibody from many fewer animals than needed with techniques now used.

At present, 100 rats are needed to produce 10⁷ lytic units of anti-Ag-B serum for example, but using the Milstein/Rajewsky approach only one rat would be needed, although perhaps 10 rats would be necessary to cover all the variants of specificity.

The commercial importance of such work is that it converts antibody production from a biological science with all its inherent variability and non-reproducibility into the realms of synthetic chemistry where any desired reagent is available off the shelf and can be assumed with reasonable confidence to be identical to the same reagent in any other laboratory. Monoclonal antibodies do have disadvantages; for example, a monoclonal anti-HLA-B7 reagent might only react with 10% of the HLA-B7 individuals defined by a polyclonal serum. Such disadvantages can be easily circumvented however, and there will be the advantage that it will be possible to identify the variants of histocompatibility specificities such as HLA-B7 so precisely that near perfect tissue matchings can be made, and the precise relationship of disease to the HLA-B7 complex defined.

The potential of cell fusion in immunology extends far beyond immunoglobulin production. It should eventually be possible to produce a range of helper, suppressor and factor-producing cell lines. The development of the Milstein technique now offers the British government a unique opportunity of extending this work by financing a centre for the production of such hybrid cell lines and for UK companies to take the commercial initiative. □