Significance of Sex Linked Antigens

THE observation that individuals of the same species may differ from each other antigenically is now so well established as to hardly bear remarking. Antigen hunting, the identification of more and more antigens, has rightly fallen into disrepute as a worthwhile activity, yet it cannot be claimed that there is any clear idea of the biological significance of the remarkable antigenic variation observed in most mammalian species.

Two extreme views for this variation can be put forward. The first is that it arises as a result of a random event, mutation, but that one form of the antigenic material confers some kind of biological advantage, and the alternative form confers another kind of advantage. Antigenic variation, as pointed out by E. B. Ford, would thus form an example of a balanced polymorphism, and takes its place with such phenomena as variation in rings on snail shells and spots on insect wings as part of a more or less homogeneous group of biological variations. On this hypothesis there is a need to look only for a cause for the maintenance of the antigenic variation, and it may be fortuitous that the variant materials are antigenic. They have a role in the cell membrane, and one antigenic form may be more advantageous in one environment than in another.

The alternative hypothesis is that it is the antigenicity of the materials which is important. There have been many hypotheses that have utilized this idea—one of the most recent is the suggestion of Jerne (*Europ. J. Immunol.*, **1**, 1; 1971) that histocompatibility antigens, such as H-2 antigens in the mouse, may play a part in the generation of immunoglobulin diversity. It has also been frequently suggested that histocompatibility antigens play a part in distinguishing neoplastic cells from normal cells, although the way in which this is done is far from clear.

These two kinds of hypothesis can, of course, be merged into one, because all variation must originate in mutation, and it can hardly be the case, for example, that the need to distinguish neoplastic and normal cells gave rise to antigenic variation—the origin of any variation must precede its utilization.

Even if this view of the origin of variation is accepted, it is still necessary to look for the reason for its survival, that is, for its "function". The direct demonstration of the mouse H-Y antigen, controlled by a gene on the Y chromosome, on mouse spermatozoa by Goldberg, Boyse, Bennett, Scheid and Carswell (see page 478 of this issue of *Nature*) puts this antigen firmly on the map as an antigenic system the biological role of which ought to be investigated. The use of skin grafts to investigate the H-Y antigen has hitherto clearly limited what could be done.

If it is acknowledged that antigen systems like H-Y in the mouse, and the human Xg^a blood group antigen (controlled by an X chromosome gene), may have biological roles, why are the genes that control them on the X or Y chromosomes? The same question can, of course, be asked of other genes present in moderately high frequency in the population, such as those on the human X chromosome which affect colour vision. One should not, perhaps, make too much of this—the X and Y chromosomes represent a considerable proportion of the animal's genetic material; that it can all be concerned with sexual differentiation seems unlikely.

Apart from these rather vague speculations, it is much easier to comment on the usefulness of these antigens to investigators. Race and Sanger, in their book *Blood Groups in Man* (Blackwell, Oxford and Edinburgh, 1968), point out how the investigation of the Xg^a blood group has revolutionized knowledge of the human X chromosome linkage group, and indeed of human genetics as a whole. The development of a direct cytotoxic test for the mouse H-Y antigen by Goldberg *et al.* could do the same for the mouse. Although many of the investigational problems which beset human genetics do not exist in the mouse, the development of a serological test will be a great spur to the investigation of the mouse Y linkage group, and it might one day lead to an answer to the question posed earlier—whether or not the H-Y gene is present on the Y chromosome fortuitously.

It is worthwhile drawing attention to another specific feature of Goldberg's work, that at least some, and

therefore possibly all, X bearing spermatozoa carry the Y antigen and thus reflect the antigenic constitution of their precursor cells rather than the capabilities of the genetic material contained in the sperm; similar observations have now been made on several antigenic systems in spermatozoa. This therefore precludes the use of an immunological method, with any antigen system so far discovered, of either distinguishing or separating X or Y bearing spermatozoa, and is unlikely to form the basis of a technique for deliberate selection of male or female offspring.

DNA REPLICATION

Selective Inhibition

from our Cell Biology Correspondent

THE substituted uracil derivative, 6(p-hydroxyphenylazo)-uracil (HPUra) is today unlikely to be found outside the laboratory of N. C. Brown in Baltimore, who since 1966 has diligently been investigating its effects on DNA synthesis and DNA replication in a variety of bacteria. But to judge from what he has to say in the *Journal of Molecular Biology* (**59**, 1; 1971), the manufacturers of this compound, Imperial Chemical Industries Limited, can anticipate a spate of begging letters. For, according to Brown, HPUra inhibits the semiconservative replication of DNA without affecting DNA repair.

During the past five years Brown has shown that although the compound selectively and reversibly inhibits DNA replication in *Bacillus subtilis* and a range of Gram positive bacteria it does not bind with great affinity to DNA, it does not stop the replication of phage in *B. subtilis*, neither does it impair transcription, translation or the synthesis of bacterial cell wall materials. Attempts to characterize the way in which the drug acts by adding it to a range of membrane fractions, preparations of *B. subtilis* exposed to lysozyme and apparently even cells made permeable by exposure to toluene, have all failed. The DNA synthesis which these systems support *in vitro*, like the replication of phage (Brown, *Proc. US Nat. Acad. Sci.*, **67**, 1454; 1971), is refractory to HPUra.

Because of this Brown was forced to re-examine the effects of this compound on intact bacteria because they alone support the DNA replication process sensitive to HPUra. He selected the strain of *B. subtilis* 168 *thy⁻ ind⁻* for this work, for as Pettijohn and Hana-