NEWS AND VIEWS

X-Chromosome Inactivation in Mules and Hinnies

ACCORDING to the inactive-*X* hypothesis of dosage compensation (Lyon, *Nature*, **190**, 372; 1962), one or other of the two *X*-chromosomes of the mammalian female becomes genetically inactivated at an early stage of embryonic development and the choice of which *X* becomes inactivated in each cell is a random one, with the result that clones of cells arise within individual females, having either the maternally-derived or paternally-derived *X* in the inactive condition. The late DNA replication of one *X*, observed in the somatic cells of female mammals, and genetic inactivity of one *X* are generally considered to be related phenomena but as yet there is no final proof of this.

Horse–donkey hybrids have two qualities which make them unique material for testing the inactive *X* hypothesis: first, the horse and donkey *X*-chromosomes are morphologically distinguishable and, second, the *X*-linked genes which code for glucose-6-phosphate dehydrogenase (G6PD) in each species show different electrophoretic mobilities. A mixed expression of horse and donkey G6PD is generally found in cell cultures from female mules and hinnies but evidence that this derives from the presence of two cell populations, one with the donkey *X* active and one with horse *X* active, has only now been obtained. Hamerton, Gianelli and co-workers in an article on page of this issue of *Nature* have shown that cloning cells from original skin fibroblasts which show mixed G6PD expression yield clones which produce either horse or donkey G6PD. A small proportion of clones showing mixed expression were also found but, on recloning, these could again be broken down into the two component cell types. These data are thus consistent with the inactive-*X* hypothesis but, although they do not disprove Grüneberg's hypothesis (*J. Embryol. Exp. Morph.*, **22**, 145; 1969) that the activity of one or other *X* may range from 0 per cent to 100 per cent of the total *X*-chromosome activity of any one cell, they make it seem most improbable that such a mechanism operates in the mule, at least *in vitro*.

An impressive inverse correlation between late replication of the horse and donkey *X*-chromosomes and horse and donkey G6PD expression has recently been demonstrated by Cohen and Rattuzzi in the female mule (*Proc. US Nat. Acad. Sci.*, **68**, 544; 1971) and the two articles by Hamerton and Giannelli on pages 312 and 315 of this issue of *Nature* amplify these findings. With both the mule and the hinny, agreement was found between the frequency of cells in original fibroblast cultures with late replicating donkey or horse *X*-chromosome and the estimated frequency of cells in these cultures expressing donkey or horse G6PD, as determined by the yield of the two cell types in cloning experiments. Final proof of a definite relationship between late replication and genetic inactivity will be obtainable when late replication of the *X* is studied in horse and donkey G6PD clones.

Perhaps the most intriguing information provided by the present studies on horse–donkey hybrids is the discovery of extensive cell selection operating both *in vitro* and *in vivo*. In the *in vitro* studies this was best seen from the results of recloning mixed clones. If it is assumed that these mixed clones originated from two cells, one with the horse *X* active and one with the donkey *X* active, the proportion of sub-clones expressing the donkey G6PD is found to be significantly lower than that expected. Whereas this observation suggests powerful selective forces acting against cells with the donkey *X* active, it would be useful to subject this interpretation to test. This could be done by cloning cultures derived from artificial mixtures of the two cell types.

Hook and Brustman's article on page 349 provides striking evidence of organ differences in G6PD expression among a very large sample of female mules. Two organ types could be identified, one in which the horse G6PD predominates and one in which horse and donkey G6PD expression is not significantly different from that expected on a random basis. Because a predominance of donkey G6PD was never consistently found in any tissue studied, these data agree with Hamerton's in suggesting that selective forces operate against cells with the donkey *X* active, at least in some tissues and organs.

Earlier studies on the female mule had shown little agreement as to the frequency with which the horse and donkey *X*-chromosomes show late replication. In the light of the new evidence it seems most probable that this only reflected inter-animal variation. This could result either from the randomness with which one or other *X* is inactivated and/or from differences in the selection forces operating upon the two cell populations in different animals. In this context it will be interesting to see if selection operates against cells with a donkey *X* active even in animals which show a predominantly donkey G6PD expression. The new data do not contribute any evidence on the randomness of the *X* inactivation process in horse–donkey hybrids though they rule out the once real possibility that the paternally-derived *X* might be preferentially inactivated in the hybrid of each reciprocal cross.

New Class of Varying Stars

FOLLOWING the discovery of X-ray pulsations from Cygnus X-1, the data collected by the Explorer 42 X-ray satellite (Uhuru) have been intensively searched for evidence of any similar pulsations in other sources. To the surprise of most astronomers—and probably to their own surprise as well—R. Giacconi, H. Gursky, E. Kellog, E. Schreier and H. Tananbaum have now found that the source Centaurus