different for these two polymers (5 Å for DNA and 2 Å for PVP), has a marked influence on the conformation of the histone. Because of the biological significance of histone-DNA complexes, the conformation of the f2a1 histone bound to DNA is of particular interest. Unlike the lysine-rich histones³, the arginine-rich f2a1 histone assumes a specific configuration on interaction with DNA. Because the arginine-rich histones have been implicated as mediators in hormonal activation of the transcription process⁴, both the conformation of the f2a1 histone bound to DNA and possible alterations in its conformation as a result of interaction with hormones is of particular interest. Further studies along these lines are now in progress.

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Expression of Malignancy in Somatic Cell Hybrids

HARRIS *et al.*¹, last year published their findings on the suppression of malignancy by cell fusion in systems involving three mouse malignant ascites tumours crossed with the A9 low malignant cell line, and this was followed by discussion between these authors and Dr Ephrussi and his associates². In their answer, Professors Harris and Klein³ refer to some of our original publications^{4,5}, in which the phenomenon of somatic cell hybridization was first described. Unfortunately, the interpretation of this work may have been ambiguous and we wish to clarify certain points which to us are important.

Harris and Klein affirm: "The article of Barski and Cornefert does not contain any data on the chromosomal constitution of the tumours produced by the injection of their hybrid cells. What is described in this article is the chromosomal constitution of two lines of cells, each derived from a single tumour, two months after the establishment of these lines *in vitro*". In reality, as we reported in the article quoted and in an earlier publication⁶, six tumours, obtained by inoculation of hybrid cells, were analysed at different times after explantation *in vitro*. Their karyotypes were identified as hybrid M type. It is true that during animal passage, but also following *in vitro* passages, a tendency for chromosome loss was observed. In some cases at least, however, this loss was limited to a few chromosomes, a phenomenon also observed to a similar extent by Harris *et al.* with their non-malignant hybrids: A9/Ehrlich and A9/SEKA. It is important to stress that a similar degree of chromosome loss was observed in the M hybrid clones, whether they were passaged as tumours in the animal or only *in vitro*. This was the case in particular for the *in vitro* clones M 6, 7, 9 and 5 (ref. 4). In some cases chromosome loss was less important *in vivo* than *in vitro*.

Thus our observations, in repeated experiments in the system we used, gave no evidence to suggest that the passage of hybrid cell populations in the animal selected

cell variants in which loss of chromosomes was paralleled by an increase of malignancy, a phenomenon now observed by Harris *et al.*¹ in their A9/malignant ascites system. Rather, the M hybrid clones preserved with remarkable constancy—indeed for years—several bi-armed chromosomes identifiable as inherited from the non-malignant N2 parent cell, together with a number of well expressed and stable phenotypic characteristics which did not exist in the malignant N1 parent cells. The principal fact, extensively documented in our articles^{4,7}, was that in spite of the variability of the hybrid karyotype, which showed a tendency for chromosome loss from the 120–125 values (representing an ideal addition of the two parental karyotypes) the malignancy of the hybrid cells, expressed as TD₅₀, or in terms of rapidity of tumour growth, was remarkably stable and approximated that of the malignant parent.

To fit the suggestion of Harris and Klein, according to which the principle of suppression of malignancy in hybrids between invasive and non-invasive cells also has to be applied to the interpretation of our results, we should have to admit that our M hybrids were non-malignant at their "birth" but became so following a chromosome loss: "the loss of a single chromosome may be enough"³. Unfortunately, this would be impossible to prove or disprove experimentally in view of the inevitable lability of chromosomes, at least those of the mouse cells used in hybridization experiments. In the absence of such proof, we are inclined to postulate, more simply and less acrobatically, that the M hybrids inherited from their malignant parent invasive properties which, in this case, were not repressed by the persistent genome of the non-malignant parent.

Although somatic cell hybridization supplied an exceptionally efficient tool for the analysis of mechanisms involved in the heredity of cell malignancy and opened "a direct biochemical approach to the mechanisms by which the malignancy is suppressed"¹, in our opinion no general rule can be formulated yet concerning the "recessiveness" or "dominancy" of cell malignancy (a cell property which can hardly be regarded as a character in the Mendelian sense).

This is borne out not only by our findings, but also by results obtained in several laboratories, some of them quoted by Harris and Klein^{8–10}, which suggest that in many other experimental systems hybrids between invasive and non-invasive cells seem consistently to have tumour producing properties. The system used by Harris *et al.*¹ is not only unique in the use of A9 cells as "suppressors" of malignancy but also because of the conditions in which the hybrids were isolated—by virtue of their capacity to grow on the glass surface which constitutes a severe preliminary selection. Indeed, this selection may eliminate possible hybrid variants which inherited from their ascites tumour parents the incapacity to grow on glass. One cannot exclude the possibility that malignancy is associated with these very hybrids.

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