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HeLa takes over

by Sandy Grimwade

ALTHOUGH it was suggested in 1967 by Gartler (*Natn. Cancer Inst. Monogr.*, **26**, 167) on the basis of isoenzyme patterns that not all cell lines in common use were what they purported to be, it was not until last year that cytogenetic studies by Nelson-Rees *et al.* (*Science*, **184**, 1093; 1974) demonstrated conclusively the extent of contamination. Gartler showed that many commonly used cell lines, supposedly of Caucasian origin, contained the A-type isoenzyme of glucose-6-phosphate dehydrogenase (G6PD), which is in fact found only in approximately 30% of the Negro race. One cell line which legitimately contains G6PD type A is the HeLa line, the oldest and most widely used of all cell cultures, which was esablished in the early 1950s from the cervical carcinoma of a Negro woman in Baltimore named Henrietta Lacks. The warning attached to that finding was that many cell lines could be contaminated with HeLa.

While identification of a single isoenzyme marker left room for doubt, the advent of chromosome-banding techniques by the trypsin–Giemsa and quinacrine mustard methods showed far more specific markers. Examination of HeLa cell chromosomes by these methods shows four unusual chromosomes formed by fusion of portions of various normal chromosomes. Although there remains some disagreement between various groups of cytogeneticists about exactly which chromosomes have fused to form the markers, there is no divergence concerning the occurrence and appearance of the markers in HeLa cells.

In 1974 Nelson-Rees *et al.* reported that several commonly used cell lines from various human sources contained HeLa marker chromosomes as well as the type A G6PD. A third indication consistent with the claim that these were HeLa cells was that no Y chromosome was present. Several of the cell lines were presumed to be of male origin, and should therefore have shown Y chromosomes, whereas HeLa cells are originally female.

The extent of the HeLa take-over of cell cultures is further documented in this issue of *Nature* (page 211) in a paper from Lavappa, Macy and Shannon from the American Type Culture Collection (ATCC). The ATCC, which preserves cultures of every imaginable microorganism and animal cell, distributes its cell lines to laboratories both in the USA and elsewhere. Several thousand samples of cell cultures are sold on a non-profit basis annually. Shortly after the introduction of the isoenzyme technique, the screening of the entire stock of human cell lines for type A G6PD was initiated and in the 1972 ATCC Registry of Animal Cell Lines 27 out of 56 lines are flagged as containing this marker isoenzyme. The paper by Lavappa *et al.* presents the first results from a cytogenetic screening programme recently initiated using the newly-available chromosome banding technique. Detailed chromosome analysis of several cell lines reveals that five of the lines, all of which bear the type A G6PD, have HeLa marker chromosomes. Since submission of the paper, several other lines have been tested, and so far all the lines with the suspect G6PD isoenzyme have also been found to bear the HeLa markers. Not all these lines have all four markers, however. Detroit 6 cells, for example, lack HeLa marker (HM) 1, but contain two copies of HM2, 3–4 copies of HM3 and show some variability in HM4. These variations are thought to have arisen by somatic cell hybridisation between the original cell line and contaminating HeLa cells. There is also the remote possibility that these markers have arisen spontaneously in more than one cell line.

The results of the ATCC survey and of several other investigations of cell lines in general use have been combined in an extensive table in a recent *Science* paper by Nelson-Rees and Flandermeyer (*Science*, **191**, 96–98; 1976). In addition to the criteria already mentioned, phosphoglucomutase izoenzyme and HLA antigen data are included. In all, more than 70 cell lines with HeLa characteristics are listed.

These results should give rise to some reappraisal of results in the many laboratories where these cultures are being used. Investigators who think they are working with liver or bone marrow, for example, may find that they have been dealing with Henrietta Lacks' extraordinary carcinoma all along.

It is interesting to speculate on the reasons for the virulence of HeLa cells and the origins of the widespread contamination. It seems reasonable to say that HeLa cells being the oldest line in existence have been subjected to the maximum selective pressure. HeLa cells have been cultured an untold number of times. Those in the ATCC have probably been passaged more than 400 times since their initial isolation in the relatively unrefined culture conditions of 1951 and are therefore perfectly adapted to laboratory conditions. The chromosome studies at the ATCC were carried out on cells passaged only once or twice from the frozen seed stock. As the cell lines now shown to be contaminated with HeLa were mostly frozen and deposited at the ATCC in the early 1960s, often after several hundred passages, the contaminations probably occurred long before their deposition at the ATCC in laboratories where more than one cell line was being handled. The basic biochemical or genetic reason for the virulence of the HeLa cells which would account for their ability to take over any cell culture remains a mystery however.

Although several of its human cell lines are now shown to be contaminated with HeLa, and up to half of them are suspect, the ATCC intends to continue carrying these lines in its catalogues. Despite the fact that the cell lines are similar in their chromosomes, they retain individual characteristics, such as growth rate and virus susceptibility, worth preserving. □

Nova Cygni 1975

from P. J. Andrews

NOVA Cygni 1975, first reported by Honda, was independently discovered by hundreds of astronomers as a bright star in the constellation Cygnus on the evening of August 29. It subsequently became the brightest nova seen since Nova Puppis 1942. First indications that the nova was unusual came when a search for the prenova on the Palomar Sky Survey plates showed no star at the nova's position. The rise in brightness, 18 mag, was greater than any previously known; in fact it led to the suggestion, subsequently refuted, that the object was a supernova.

The most widely held theory for the nova phenomenon is that the prenova is a close binary system consisting of a red dwarf, which is filling its Roche Lobe, spilling matter over towards a white dwarf companion. The period of the binary is shorter for systems containing fainter, cooler red dwarfs. The nova outburst is believed to be due to the flow of material from the red star passing by way of an accretion disk to the white dwarf's atmosphere where it is compressed and heated by the gravitational field until it reaches the ignition temperature for hydrogen burning reactions. Once ignition occurs there is a thermonuclear runaway generating the necessary energy to produce the very hot expanding shell of gas which is seen as the nova eruption.

The development of the nova is the evolution of this expanding region. In general the development is complex with several different systems of absorp-