# HeLa, a new microbial species[1]

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Received 7 January 1991; 1 March 1991

ABSTRACT: Consistent application of our criteria for species seems to require that HeLa cells, a vigorous clone of human origin, be regarded as a separate species. We propose new taxa for it to the level of family. This species has been unusually successful in its niche, but the existence of other, less extreme, examples raises several problems which await resolution. Our concepts should incorporate the diversity of real phenomena.

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Species originate in diverse ways. HeLa cells are the best-known cultured cells of human origin, We here propose, in all seriousness, that they have become a separate species restricted to a particular environment.

First, some background. (Gold [1986] has provided an accessible account from which much of the information about the species can be retrieved. We have not cited earlier work with respect to information given there, although we have read various original papers and in fact had included a shorter version of this paper in an unpublished longer manuscript before his book appeared.) HeLa cells originated from a cervical adenocarcinoma in a woman named Henrietta Lacks in 1951. The tumor itself was unusually vigorous and vascularized for that region, perhaps in part because of its origin from glandular tissue. and it metastasized rapidly. As was the case for various other tumors from different people, it was sampled and grown in tissue culture. Unlike previous samples from human tumors, this sample survived and continued to grow vigorously.

Tumors from several rodents had previously been cultured successfully, and the means by which this occurred was understood in outline. Most cells don't provide good culture material. Sevim and Parker (1957) and Hayflick and Moorhead (1961) had shown that after about 50 replications human cells die out, as if they were programmed to do so. Whether this is really intrinsic, a program or a program-like running down, as Hayflick and Moorhead thought, or is a result of within-culture selection for short-term advantage at the expense of long-term survival, may still not be resolved, although Hayflick (1988) has given several lines of evidence for a program-like cause. A process called immortalization occurs occasionally, and in such cultures the cells do not die out but continue to grow indefinitely if provided with adequate resources. When immortalized cells are injected into compatible hosts, they produce cancers. Immortalization is correlated with, and may be caused by, gross changes in the genome, most obviously in the number and organization of chromosomes. Because

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[1]Contribution 107, Lothlorien Laboratory of Evolutionary Biology.
Evolutionary Theory 10: 71-74 (December, 1991).
The editors thank two referees for help in evaluating this paper.

of the number of changes involved, it is likely that immortalized cell lines are true clones, each derived from a single cell, rather than polyclones, derived from parallel changes in a larger set of cells.

The chromosomal changes provide useful markers for cell lines, as do polymorphic genes. In particular, they unambiguously identify HeLa cells.

HeLa cells turned out to be remarkably successful in the tissue-culture niche. Within a few years they had invaded and outcompeted many other cell lines, worldwide, without this having been recognized at all. Their dispersal from one culture to another occurs by means which would have delighted Darwin, who fretted over dispersal of nonflying organisms to distant islands and the like. It wasn't until 1966 that Stanley Gartler discovered the existence of the contamination of other cultures. His discovery wasn't received with open arms at a meeting that year of tissue culturists, but others have extended it. There has been some differentiation among strains of HeLa cells kept in different places (Nelson-Rees et al., 1980), as commonly occurs among geographically separated populations of a species.

So that's what HeLa cells are. (We give some technical details below.) Why on Earth call them a new species? Surely they are just fragments of Homo sapiens.

We call them a new species for four reasons. First, their genotype is very different, far outside the range of those of viable humans. Second, they occupy an ecological niche extremely different from that of humans. Third, they persist and expand well beyond the desires of the human cultivators of cells; they are the weeds of cell culture. Of course they can't interbreed with humans, but we don't emphasize this criterion in that way because individual cells of diverse vertebrates can hybridize with some cancer cells (e.g., Klinger et al., 1978); hybridomas are the result and have some fame in biotechnology. HeLa cells have been claimed to have hybridized with some other cell lines while taking them over (Lavappa, Macy, and Shannon, 1976), but there is evidence against this (Nelson-Rees et al., 1980). It is neverheless relevant that HeLa cells don't exchange genes with real humans.

HeLa cells depend for their existence on the continuation of the practice of tissue culture. Their niche is wholely artificial and its indefinite perpetuation is, we suppose, unlikely. So what? Human-created habitats now cover a too-large part of the Earth's habitable land, and many species have taken advantage of this new set of habitats. And the expected persistence of its habitat is never used as a criterion for judging the reality of a species, but rather for judging its susceptibility to extinction.

That HeLa cells came from Homo sapiens is in itself no more an argument against their status as a separate species than would be the same argument applied to H. sapiens as having come from H. erectus. The mode of speciation is different, and it is not one that is conventionally recognized. The speciation even occurred as a result of deliberate human action. We recognize, though, that other species have originated by even more deliberate human action, namely hybridization to produce polyploids, some of which have even re-originated species pre-existing in nature. If we don't recognize a mode of speciation, perhaps that's an indication to get acquainted with it.

HeLa cells now have an evolution quite independent of that of Homo sapiens, except for their niche dependence, which is an entirely different matter. This evolutionary independence from other species,

together with a degree of unity within the species, is the basic idea underlying our various formulations and gropings at definitions of what species are. HeLa cells fully satisfy this basic notion. They are unconventional, as a species, but so were, e.g., sib species once. The problem is with our perceptions, not with the phenomena.

Regarding HeLa cells as a separate species opens several cans of worms. Most obviously, perhaps, how should this species be classified? Its way of life has no resemblance to that of, say, mammals, but is instead convergent on that of amoebas. It obviously can't be classified with amoebas, however, because of its entirely different origin. We leave this question open and don't specify taxa above the family level.

There are other immortalized cell lines, not as weedy as HeLa but still as divergent from their multicelled ancestors. They come from diverse origins within and among species. What should be done with them? We leave this question open too.

This is related to a question which has been ignored in another context, namely the position of selfish entities within the bodies of multicellular organisms. We now conventionally regard viruses as distinct organisms, correctly in our view, but they don't differ much from some transposable elements. At another level, a cancer is a selfish group of cells, successful in competition on a short time scale. Such phenomena are diverse and deserve consideration from an evolutionary perspective (cf. Buss, 1988; Van Valen, 1988).

Most concepts and entities in the real world have fuzzy boundaries. Sometimes even approximate boundaries can be made only by convention. We mean here to raise what seem to us to be real problems. We propose a solution to one, where the phenomenon is well defined; other solutions may be better in other cases or even in this one. Dogma hides choices. Moreover, pigeonholing is a form of stereotypy. We should try not to force real phenomena into predefined categories, but rather let our categories evolve with our knowledge.

**Helacytidae**, new family

Type and only referred genus: *Helacyton*, new genus.
Diagnosis: For now, with the characters of *Helacyton*.

*Helacyton*, new genus

Type and only referred species: *H. gartleri*, new species.
Diagnosis: For now, with the characters of *H. gartleri*.
Etymology: HeLa cells (themselves named for Henrietta Lacks), and Greek *cytos*, cavity, or cell. Coincidentally, the Greek word *helos*, the usual meaning of which is metal nail, has a secondary meaning of callus, a suitable description of a cell culture. The gender, like that of *cytos*, is neuter. The name *Hela* is preoccupied by a crustacean.

*Helacyton gartleri*, new species

Type specimen: The HeLa cell line at the American Type Culture Collection (ATCC-CCL 2).
Diagnosis: Cells with epithelial-like morphology and unorganized monolayers of such cells, with predominantly human genotype, type A electrophoretic mobility of glucose-6-phosphate dehydrogenase and of 6-phosphogluconate dehydrogenase; type 1 mobility of esterase D, peptidase D, adenosine deaminase, and loci 1 and 3 of

phosphoglucomutase; type 2 mobility of glyoxylase locus 1; unreactive to HL-A antigen; heteroploid and approximately triploid, chromosome counts varying from 43 to 88 and modal numbers from 65 to 82; Y chromosome absent; chromosome 3 absent or monosomic; usually 1 to 5 microchromosomes per cell; unusual to unique marker chromosomes present, interpretations of the origins of which have been controversial (e.g., Heneen, 1976, who illustrates them; Lavappa, Macy, and Shannon, 1976). Other references contributing to this diagnosis are Miller et al. (1971), Nelson-Rees and Flandermeyer (1976), and Nelson-Rees et al. (1980).

Etymology: For Stanley M. Gartler, who discovered the remarkable competitive success of this species.

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