Parasitic protist of metazoan origin

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ABSTRACT: Based on various criteria for species, Van Valen and Maiorana (1991), in an article entitled "HeLa, a new microbial species," propose that *in vitro* culture of somatic cells of metazoan origin such as HeLa cells be regarded as a separate species in new taxa at the level of family. While their criteria for regarding HeLa cells as a separate species are challenging and open to debate and question, the concept is of interest because immortal somatic cells of metazoa do exist and are propagated not only in artificial culture dish but also in nature through transmission from generation to generation among members of the species and, even, family of origin.

In this communication, we describe such a unique model, the canine transmissible venereal sarcoma (CTVS) which represents a contagious protist that "jumps out" of its original metazoan host, the dog, *Canis familaris*, parasitizes members of the Family Canis and perpetuates itself as monocellular organism, the protist.

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The third biologic kingdom, the Protista as defined by Haeckel represents non-plant and non-animal organisms with fundamentally single-celled organization (Davis et al., 1980). Some protists do form large multicellular structures such as seaweeds (marine algae) and mushrooms (basidiomycetes), they are aggregates of similar cells with only very primitive differentiation which is basically different from that of metazoans of plant and animal kingdoms with differentiated multi-cellular adult forms reproducing via transient unicellular gametes. These single-celled gametes, such as sperms, are haploids which survive only for a certain period of time in the genital organs of other members of the same species before eventually fused with the female gametes and, therefore, are not true free-living or parasitic single somatic cells similar to a protist.

Under artificial conditions, somatic cells of metazoa can be grown in *in vitro* culture as single cells similar to protists but they generally are not capable of growing *in vivo* in other members of the same species (allogeneic) or other species (xenogeneic) unless the hosts are genetically identical (inbred or at least histocompatible) or immunodeficient (athymic or severe combined immunodeficiency). Similarly, cancer cells arise in vivo in a metazoan host die with the host and, as a rule, can not be inheritably propagated beyond the originating host in nature.

Based on various criteria for species, however, Van Valen and Maiorana (1991), in an article entitled "HeLa, a new microbial species," propose that *in vitro* culture of somatic cells of metazoan origin such as HeLa cells be regarded as a separate species in new taxa at the level of family. The criteria include: (1) their unique genotype which is very different from that of viable

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humans: (2) their occupation of an ecological niche extremely different from that of humans; (3) their persistent proliferative capacity; and (4) their independence for exchanging genes, i.e., interbreeding with humans.

While their criteria for regarding HeLa cells as a separate species are challenging and open to debate and question, it is of interest because immortal fragments of metazoa exist and are perpetuating themselves as a parasitic monocellular organism protist, among normal metazoan members of the species and, even, family of origin.

In this communication, we present a unique example of the experiment of Nature representing a "parasitic" protist of metazoan origin, the canine transmissible venereal sarcoma (CTVS).

The CTVS, also called transmissible venereal tumor (TVT) and Sticker's sarcoma, is a naturally occurring contagious neoplasm of the external genitalia of dogs (Figure 1) which is transmitted through sexual contact or laboratory transplantation with intact viable cells. Historically, it is the first tumor ever to be transplanted from one animal to another (Novinsky, 1876; Shimkin, 1955). It is transplantable as a whole cell, but not as cell-free-extracts, across major histocompatibility (MHC) barriers among dogs and even other members of the canine family, such as wolves, foxes, coyotes, and jackals (Sticker, 1906; Wade, 1908; Gross, 1983; Cohen, 1985). Following transplantation, CTVS grows progressively for 2-4 months and then spontaneously regresses in adult dogs but metastasizes in neonatally inoculated puppies (Yang and Jones, 1973) or immunosuppressed dogs (Cohen, 1973). The mechanisms of how the tumor cells manage to overcome host's defence so successfully for such a long period of time and yet succumb later are not known (Cohen, 1985; Yang, 1987; Yang et al. 1991).

CTVS occurs worldwide in geographic regions where dogs are allowed to roam freely. Although the chromosomes of the tumor deviate greatly from normal dog complements of 76 acrocentric autosomes and 2 submetacentric sex chromosomes, the chromosome complements found in tumor samples from different continents, e.g., Japan (Takayama, 1958; Makino, 1963), Europe (Barski and Cornefert-Jensen, 1966), and the Americas (Weber et al. 1965; Thorburn et al. 1968) are strikingly similar and deviate only slightly from each other in stemline patterns. Seventeen tumors studied by Makino (1963) in Japan had modal number of 59, containing 17 metacentrics or submetacentrics and 42 acrocentrics. Similarly, 2 cases, one primary and one transplanted, reported by Weber et al. (1965) in the U. S. also had modal number of 59, containing 15 metacentrics or submetacentrics and 44 acrocentrics. In addition, many of the tumors studied had a large heteropyknotic submetacentric marker (Weber et al. 1965; Thorburn et al. 1968; Oshimura et al. 1973). Although tumors with slightly different chromosome numbers occur rarely, most tumors had a very similar stemline (Makino, 1963).

It is not known whether the karyotypic change reflects gene arrangements specific to the malignant growth and unique tumor behaviour or general preference for specific karyotypic remodeling or selection against nonspecific chromosomal alterations during tumor progression (Mori, 1969; Sonoda et al., 1970; Cohen, 1985) the findings suggest that although the etiology is not known, CTVS might have originated in a single dog over a century ago and, through subsequent selection during tumor progression, has become a naturally transplantable tumor stemline (Novinsky, 1876; Makino, 1963).

It is certain also that the unique karyotype is not induced in every tumor *de novo*, substantiating the stem line hypothesis of tumor transmission in CTVS (Makino, 1963). In addition tumor samples from various geographic locations have been shown to have the common tumor-associated antigen (Palker and Yang, 1981) and the same LINE insert upstream to c-myc (Katzir et al. 1987). CTVS thus represents a contagious single-celled protist that "jumps out" from its original metazoan host the *Canis familaris*, transmitted through sexual contact and parasitizes in members of the species.

Although there are many experimental tumors which are also allotransplantable and even xenotransplantable through human intervention, to our knowledge there is only one other naturally transplantable tumor the reticulum cell sarcoma of the Syrian hamster reported by Brindley and Banfield (1961). It also arose spontaneously in one animal, is naturally contagious through oral transmission and shows a consistent markedly abnormal chromosome elements strikingly different from the normal hamster karyotype (Cooper et al. 1964).

Although presently without known counterpart in man, Stein reported potential transmission of genital tumors between a husband and wife (Stein, 1980) and possibility of transmission of Kaposi's sarcoma among AIDS or immunosuppressed patients can not be excluded.

These naturally occurring contagious tumors may thus represent a new taxa (phylum) of semi-free-living (parasitic) metazoan somatic cells of animal kingdom origin. Although they behave as parasitic protists, they have mitochondria and other organelles unique to their metazoan hosts of origin.

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Contagious Somatic Cells

Figure 1. Penile and preputial tumor masses with metastasis to superficial inguinal lymph nodes.