Tobacco Documents Online

Smokefree Network Login:

[SIGN UP]

your email
Email

Password

LOGIN
(Forgot Password?)

- Home
- Collections
- Profiles
- More
- Recent Searches

Jump to: - CTR

Council for Tobacco Research

"Inherited "Switched-Off" Rna Tumor Virus Oncogenes As Determinants of Cancer" [St Discusses Cells of Probably All Vertebrates As Having Rna Virus Genomes of C-Type Transmitted As Part of Normal Inheritance]

Date: Dec 1969 (est.)
Length: 2 pages
11317536-11317537
Jump To Images

http://tobaccodocuments.org/ctr/11317536-7537.html
snapshot_ctr 11317536_7537

Abstract

MIS;MAR

Fields

Type
SCIENTIFIC ARTICLE
Master ID
11317536-7537
Request
4
Depository Date
27 Nov 1996
Named Person
Th
Intl Union Against Cancer Bulletin
Proceedings, O.F. The Natl Academy, O.F. Sciences
Aaronson
Ageenko, A.I.
Fischinger
Freeman
Gross, L.
Hartley
Jacob
Kaplan, H.
Lwoff, A.
Monod
Oconnor
Old
Price
Sarma
Todaro, G.
Zilber, L.A.
Author
Huebner, R.J.
Box
213
UCSF Legacy ID

mri6aa00

Document Images

Text Control

☐ Hide Citation (above)

Highlight Text:

OCR Text Alignment:
- Select one -

Image Control

Image Rotation:
None

Image Size:
750 Pixels

Document Navigation

View Range: 1 - 2 of 2

REDISPLAY

Page 1: 11317536_7537 Log in for more options!

Recently George Todaro and I submitted a paper for publication in the Proceedings of the National Academy of Sciences of the United States of America, enti- fled, "Oncogenes of RNA Tumor Viruses as Deter- minants of Cancer", in which we postulated that cells of probably all vertebrates have RNA virus genomes of the C-type* that are transmitted from parent to offspring (and from cell to daughter cell) as part of normal inheritance. Host regulator genes and repres- sors and various environmental carcinogens are viewed as controlling the expressions of the onco- gene(s) and virogene(s) of the vertically transmitted viral genome. This hypothesis implies that cancer is a natural biological event determined by spontaneous and/0r induced derepression of u'niversally or highly ,rl'h~ prdli~type,~ late th~'"a~'i~n ! sarComa v[ras 'described by' Rio~,s '~n,d thl~ murkne leukemia virus described by Gross. prevalent specific .viral oncogenes, thus providing a rational basis for a unifying theory of cancer which is

consistent with the ptlenomelaon of naturally oc.curring cancers, as well as with radiation, chemical- and viral- induced cancers. The basic concepts of this hypothesis are not al- together new. Henry Kaplan, Ludwik Gross, A. I. Ageenko and L.A. Zilber each postulated activation of latent viruses as likely explanations of the trans- missible leukemias and sarcomas they induced in mice by radiation or carcinogenic chemicals. Andre Lwoff in a 1960 Rye Conference proposed that the observa- tions by Jacob and Monod in the bacterial cell model system may apply to the cancer problem. According to this view, the expressions of cancer virus genes (operons), like other genes, would b.e controlled by a system of repressors coded for by regulator genes in the o~k Th~ view further implies that genetic defects, mutations, inducing agents such as radiation, carci- nogens and mutagens, and f'mally simply the aging process itself lead to decreased repression of the viral oncogene(s). Other host factors in cancer, such as the immunological and hormonal systems, are also con- trolled by cell gene regulators and are clearly addi- tional rather well-defined determinants of the clinical entity called cancer. Obviously a broad concept of the actuating cause of cancer such as we are proposing requires a great deal more substantiation than is now available before it can be fully accepted as the explanation for the generality of cancer. However, we believe the hypo- thesis has heuristic value in that it can now be tested exhaustively in a variety of animal species and, we

Page 2: 11317536_7537 Log in for more options!

hope, very soon in man. Our hypothesis derives from the twin facts that these viruses have been found in almost all species so far examined'and that they have a proven role as natural causative agents in certain animal spet ies, and presumptive roles in many others. Recent studies show that the RNA virus genomes of the C-type are unique enough and prevalent enough in mice, chickens and cats to account for the gener- ality of cancers in these species. C-type RNA viruses have also been demonstrated in hamsters and rats and have been seen by electron microscopy in tumor cells of cattle, swine, guinea-pigs, snakes, monkeys and humans; thus, 11 species.and three classes of verte- brates, actually all those given Simply a reasonable amount of study, have been shown to harbor the C-type RNA virus genome. I cannot in a brief note such as this provide all the hvailable substantiating evidence for our hypothesis (several definitive papers are in press). In short, how- ever, the current data indicate that the C-type RNA virus genomes are : (1) Established determinants of naturally occurring leukemias and sarcomas of tnice, chickens and cats, and lymphomas in hamsters, and presumptive determinants of carcinomas in these species. Biological necessities and the presence of these unique particles suggest that other species, including monkey and human, will have similar determinants.. (2) Vertically transmitted and generally switched off for virogenic and oncogenic activity in most non-inbred animals. Tests for group-specific (GS) and envelope (G+) antigens (developed only recently by Huebner, Hartley and associates and by Old and associates) have shown the presence of the viral genome in tu- mors and normal tissues free of infectious virus. Wild feral mice are a perfect case in point; 3% have even partial expression of the virus in earl~ and mid- life, but virus is often switched on when tumors are induced by chemicals. Lifetime studies of various strains or colonies of laboratory mice and chickens have revealed switch-on of GS antigen correlated with spontaneous tumors more often than not in the absence Of easily demonstrated infectious virus. In all inbred strains of mice which have high incidences of early leukemia large amounts of RNA virus expression can be demonstrated at all times beginning at birth, and the vktr, e~ f~rom ~ese 5tmi~ inoeu.lated into susceptible strains produce lymphomas and other tumors. Perhaps the most direct evidence of switch-on was provided by Aaronson, Hartley and Torado who observed

spontaneous emergence of the C-type viru- ses, after numerous cell cultures, in embryo cells from two switched-off strains of mice. (3) Determinants of radiation and chemically induced cancer in low incidence cancer (switched-of.l) strains of mice. The GS antigens of the RNA virus are frequently switched on in the induced tumors of mice; only rarely is the association 100°7o. Altough infectious virus, antigen and tumor expressions have separate oncogene determinants and probably distinct re- pressors, the switch-on by radiation and chemical car- cinogens is predictable and reproducible in many differents strains of mice. Our recent findings, as well as the prior evidence of Gross, Kaplan and Ageenko, indicate that infectious lymphoma- and sarcoma- inducing viruses can be demonstrated in many such tumors .ipmb, ided. suitable genetically susgeptible reci- pients are injected at birth With cell-free' extracts' and if necessary by holding the mice for 12 to 18 months cw even lanffer. (4) Detertninants of defective (noninfectious) movablk sarcoma on~ogenes found in virus-free tumors. Defective chicken, mouse and cat sarcoma genomes can be rescued by homotypic and heterotypic C-type RNA viruses and then. can be transmitted to a variety of heterotypic species as well as to differing homo- typic strains. To give an example, Fischinger and O'Connor and Sarnaa have shown that the "movable'" noninfectious cancer genome of the mouse sarcoma can be rescued by cat lymphoma virus following which it will infect and transform not only cat but .also dog and human cells. (5) Determinaitts of spontaneous and chemicall); induced transformation of normal cells grown in vitro. Aaronson" and Todaro reported spontaneous trans- formation correlated with the emergence of virus in BALB/c and Swiss mouse embryo cells (mentioned above). Freeman and Price have subsequently pro- duced early transformation of normal rat cells in- fected with murine C-type viruses when also treated with 0.1 ugrn of 3-methylcholanthrene. Neither factor alone produced transformation despite numerous sub- cultures (> 50). Extensions of these studies to mouse cells carrying endogenous RNA genomes show that even when the virus is only partially expressed this expression leads to accelerated transfomaation by very small amounts of chemical carcinogens. (6) Determinants of DNA virus cell transformatior~. Stenbach and others have shown by electron microscopy that hamster tumors induced by adeno- virus and SV40 contain C-type RNA viruses. Simi- larly, mouse cells transformed in vitro by SV40 have been found to have similarly switched-on C-type RNA .viruses. Price and Freeman have shown that adencwirus transformation, of mt ceils is great!y accelerated by pre-infection with murine leukemia viruses as in (5) above. (7) Determinants of tolerance for homotypic anti- body to GS antigen in all individual animals so far studied (mice, chickens and cats). This may prove to be one of the more conclusive arguments in favor of our hypothesis. Although not tolerant to other viruses and/or to the envelope of their own C-type virus, all or virtually al'l individual ~ (mice, cats. ~nd chickens) having high titer~ of GS. antigen in their normal or tumored tissues fail to develop any detectable antNodies to them. This implies not only universal expression of the RNA genome in the early embryo, thus confirming vertical transmission of the genome, but it also suggests that the RNA virus genome and GS antigen expression may have a function in the early development of the embryo. This observation, which is true for mice, chickens and cats, if confirmed for other species, may explain the observation made years ago that certain cancers have internal cell antigens identical to those found in the primordial embryonic organ involved with the cancer. Finally, the prospect of achieving better under- standing of how normal cells and normal animals succeed in preventing expression of identifiable endo- genous viral oncogenes (we view them as cancer • genes with handles on them) offers an entirely new', and I believe hopeful, approach to the eventual con-trol of cancer. (Summaries on page 3) I~

Text Control

☐ Hide Citation (above)

Highlight Text:

OCR Text Alignment:
- Select one -

Image Control

Image Rotation:
None

Image Size:
750 Pixels

Document Navigation

View Range: 1 - 2 of 2

REDISPLAY
