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GORDON M. TOMKINS, San Francisco Medical Center, University of California, San Francisco, California: Censorship of Genetic Information: Gene Regulation in Mammalian Cells.

SOL SPIEGELMAN, College of Physicians and Surgeons of Columbia University, New York, New York: A Molecular Approach to the Oncogenic RNA Viruses.

MAURICE GREEN, St. Louis University School of Medicine, St. Louis, Missouri: DNA and RNA Viral Gene Expression in Cell Transformation and Cancer.

ROBERT J. HUEBNER, National Institutes of Health, Bethesda, Maryland: Is Cancer Due to an Inherited RNA Viral Genome?

PETER BENTVELZEN, Radiobiological Institute of the Organization for Health Research TNO, Rijswijk, The Netherlands: Genetic Transmission of Mammary Tumor-Inciting Viruses in Mice.

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Group-Specific Antigen Expression During Embryogenesis of the Genome of the C-Type RNA Tumor Virus: Implications for Ontogenesis and Oncogenesis

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Abstract. Tests for the group-specific antigen of the C-type RNA tumor virus showed that mouse embryos of all strains tested, at some stage of development *in utero*, revealed detectable titers of group-specific antigen in one or more of their tissues; younger, rather than older, embryos were likely to be positive, particularly in those strains which normally reveal little or no expression of the RNA genome postnatally. The antigens were found in embryos of low-leukemia strains, free of infectious virus. These new findings support a previously stated hypothesis that the genome of RNA tumor viruses, mostly switched off for infectious virus expression, is vertically transmitted as part of the natural genetic apparatus of normal mouse cells. Since group-specific antigens have also been described in chick embryos and immunological tolerance to homologous group-specific antigens has been demonstrated in hamsters and cats as well as in mice and chickens, the hypothesis has been extended to include vertebrate cells in general. Finally, the high incidence and titers of the group-specific antigen suggest that the genes for RNA tumor virus, which later in life act as determinants of cancer, may be important also as gene determinants in the developing embryo.

Recently we suggested that endogenous, vertically transmitted, RNA tumor virus genomes serve as specific determinants for the generality of cancer in vertebrates. This hypothesis furnished a basis for a unitary theory capable of explaining spontaneous cancers as well as those induced by physical, chemical, hormonal, and viral agents. We envisioned the virogene and oncogene expressions as subject to regulatory host-cell genes.[1–3]

Studies of cancer incidences have revealed a stochastic pattern, not only in man and his domestic animals, but also in those laboratory species most used for

cancer research (mice, hamsters, rats, and chickens).[2,4-6] Thus, in studies of sufficiently large populations, the incidences of most, if not all, types of cancers show predictably similar patterns during many succeeding months and years, revealing differences, which are also predictable, according to sex, racial, ethnic, and geographic factors. With the exception of Burkitt's lymphoma, a quite unrepresentative clinical entity, no clustering of the kind expected of transmissible disease has been established for cancer.[7,8] Similarly, cancers induced by radiation and chemicals in experimental animals are quite predictable when dosages or exposures are well controlled and the populations are carefully observed. These observations, we believe, exclude conventional, horizontally spread, infectious viruses as serious candidates as etiologic agents for the generality of cancer.

It seemed to us, as also to workers in chemical carcinogenesis[9,10] and molecular biology,[11,12] that the persistently altered traits exhibited by neoplastic cells represented genetic activity, most probably the result of a breakdown, for whatever reason, in host-cell regulator genes leading to derepression of specific oncogenes (operons) in the involved cells.

In previous publications,[1-3,13] and in some still to be published,[14,15] we have presented data on the "switching on" of expression of group-specific (gs) antigen of the C-type tumor virus in many spontaneous and induced lymphomas and solid tumors of mice, hamsters, and cats; the antigens were demonstrated directly in the tumor tissues. In the case of subcutaneous sarcomas induced by chemicals, the adjacent normal mesenchymal tissues were completely negative. This indicated that derepression of the RNA-virus genome took place specifically in the locally induced sarcoma cells, an observation confirmed and extended by *in vitro* cultures of the tumor cells.[16,17]

Natural history studies of the prevalence of gs antigen in virus-free laboratory mice revealed gs antigens in high titers in the hematopoietic tissues of individuals of most mice strains.[2,3,18] Some laboratory strains and wild (feral) mice, however, revealed a general absence of such antigens, particularly during the early and middle parts of postnatal life.[2,17-19] The gs antigen was expressed more frequently, however, later in life; the extent of expression increasing with age, frequently correlated later in life with increasing incidence of a wide variety of spontaneous cancers.[17,20]

Of critical importance to our basic concept was the documented influence of identifiable host genes on the virogenic and oncogenic expressions of endogenous RNA tumor-virus genomes in inbred mice and chickens. Recently Payne and Chubb, working with inbred chickens,[21] and Meier, Taylor, and Myers, working with inbred mice,[22] presented evidence that gs antigen expression in both species is regulated by a dominant gene. Previously, Tennant and Snell[23] and Lilly[24] reported that differing alleles on the H_2 transplantation-antigen locus also greatly influenced the leukemia and sarcoma expressions of RNA viral genome expressions in induced tumors, while Meier *et al.*[25] described autosomal recessive genes in the hairless mouse as critical determinants of an early high incidence (45%) of lymphoma. These and other known interactions between RNA tumor virus genomes and host cell genes[25] we believe provide compelling

reasons for invoking the Jacob and Monod theory[26] of viral genome (operon) control by regulator gene repressors as a working hypothesis to explain the switching on and off of C-type RNA tumor virus expressions.

It is quite apparent from recent extensive natural history studies of the C-type RNA genome that the most frequent state of the genome in most laboratory animals during postnatal life is that of a partial or completely repressed genome. We envision that when the specific operator oncogenes of the RNA virus are derepressed spontaneously during the aging process or by chemicals and/or radiation, gene activity and cancers may occur. Although controlled by different host cell genes, the virogenes may also be derepressed, their expressions being manifest most commonly by switching on the gs antigen in the tumor cells; although infectious virus can sometimes be demonstrated, it has been usually found in small quantities and far less frequently. The relative rarity of demonstrable infectious virus possibly explains the difficulties encountered by most workers in transmitting specific tumor virus effects.[9,10]

It should be emphasized that our basic hypothesis is not altogether new, since vertical transmissions of "latent" RNA tumor viruses were invoked by Gross,[27] Kaplan,[28] and Bentvelzen[29] to explain the transmissible murine lymphomas and mammary carcinomas induced by radiation, chemicals, and hormones. It is important to recognize, however, that certain inbred mice with well-known genetic characteristics were apparently required in order to regularly demonstrate the infectious tumor viruses. Our hypothesis is significantly different in specifying that the RNA virus genome responsible for gs antigen, infectious virus, and tumor expressions are essentially part of the inherited gene pool (presumably DNA) in all the cells of normal vertebrates.[1,2] Thus, while certain well established and fully infectious RNA tumor viruses, such as the Rous and Gross prototypes, can in highly specific circumstances be manipulated by virologists to produce certain specific cancers, it has long been obvious to most cancer investigators that horizontal transmission of such viruses cannot explain either the natural prevalences of the subinfectious RNA virus genomes described above or spontaneous and chemically induced cancers.

Vertical Transmission of the RNA Genome and gs Antigen Expression during Embryogenesis. In order to substantiate our main hypothesis, it was necessary first of all to ask two questions: (1) Is the RNA genome transmitted vertically as a covert virus particle, in a manner exemplified by vertical infections of mice with cytomegalovirus and lymphocytic choriomenigitis?[30,31] or (2) Is the genome transmitted as part of the naturally inherited gene apparatus? In this report we present and discuss some recent findings which indicate that high titered expressions of the gs antigen of the RNA virus are demonstrable by complement-fixation and gel diffusion in most or all developing mouse embryos.

The gs antigen has been found expressed in normal and tumor tissues of mice, chickens, hamsters, and cats far more frequently than infectious virus; in many strains of mice, including wild feral mice which do not manifest infectious virus, it represents the only satisfactory marker or handle for the presence of the RNA virus genome.

Properties of gs Antigen. The group-specific (gs) antigen proteins of the

avian, murine, feline, and hamster C-type RNA tumor viruses have been demonstrated and to a considerable extent purified and defined.[13,32-43] Unlike the external envelope antigens which are type-specific,[38,44] the major component of the gs antigen makes up a significant portion of the nucleoid protein coat of the various C-type RNA tumor viruses. Although distinct for each of the four species, they are shared by all the C-type viruses known to occur in each of the respective species. Partial sharing of gs antigens among animal species was recently reported by Geering *et al.*[45] The antigens are most generally found in the cytoplasm, and specific antibodies to the gs antigens (which are produced in heterologous hosts) do not neutralize their corresponding infectious viruses. In cells producing infectious RNA tumor virus, the subunit gs antigens are generally made in great excess of that utilized for virion assembly; they are "soluble" in that when dispersed (i.e., not assembled in the viron nucleoid) they have a molecular weight of approximately 25,000 to 36,000.[39] Unlike the envelope antigens, they are resistant to extraction with ether and when highly purified to heat (78°C).[33,37]

The procedures most commonly used to demonstrate gs antigens are the microtiter complement-fixation (CF), fluorescent antibody (FA), and gel diffusion (gd) tests; the serological tests for the gs antigen provide also the indicator systems for the COFAL,[34] COMUL,[46] and COCAL[43] tests, used for isolating infectious avian, murine, and feline C-type RNA viruses. Since the natural hosts of each of the C-type viruses are immunologically tolerant to the gs antigen of their own C-type virus, as described in a recent communication,[3] the antisera used to detect gs antigens in every instance have been made in heterologous animal systems, i.e., in species other than those homotypic with the virus. Thus hamsters, rats, rabbits, and guinea pigs have been utilized as heterotypic host systems for the production of specific complement-fixing antibodies to the gs antigens of the various RNA tumor viruses.

In our experience, whenever sensitive and highly specific antisera are available, the most useful test for C-type RNA virus genome expression in natural host tissues has been the direct test for gs antigens;[18,21,32,34,38] extensive tests for this antigen in the murine and avian species[2,14,17,18,32,34,46-48] have revealed widespread expression of gs antigens in normal hematopoietic and hepatic tissues as well as in tumorous tissue; of importance is the fact that it was demonstrated frequently in tissues of animals which are negative for infectious virus throughout their lifetime.

Materials and Methods. Testing embryonic tissues for gs antigen: The methods used were those described for various postnatal normal and tumor tissues.[46,38] Spleens, thymuses, and livers from mothers, embryos, and newborns were removed, made into 10% extracts, sonicated, and then clarified as described previously. Embryos under 12–14 days in term were prepared *in toto:* generally each type of tissue from the embryos of a single litter were made into pools prior to processing and testing for antigen. Since gs antigens in early relatively undifferentiated embryonic tissues were less stable than those in older differentiated embryos and newborns,[49] it was necessary to process them very rapidly in the cold following which they were quick frozen and maintained at −70°C or in nitrogen freezers until tested by complement-fixation. The microtiter CF procedure described in our previous reports was employed throughout.[32,50]

Procedures for preparing antigens for gel diffusion: Purified and concentrated gs antigen used as the standard control was prepared from banded AKR virus grown in a continuous rat lymphosarcoma cell line as described in a previous report.[41] Frozen whole young embryos, and spleen, thymus, and liver of 18- to 19-day embryos and newborns were made into 20% w/v suspensions with a Ten Broeck homogenizer, using buffered saline (0.01 M Tris·HCl, pH 7.4, containing 0.1 M NaCl) as diluent. The homogenate was then sonicated in a Branson sonifier five times for 10 sec. Frozen mouse tumors originally induced by 3-methycholanthrene and derived from various strains of mice were prepared by a similar procedure. All the above operations were carried out at 4°C. Aliquots were treated with either Tween–ether (0.3M Tween 80 and 4 volumes of ether) for 10 min at room temperature or by a deoxycholate (DOC) (0.25% final concentration) genetron-113 sequential procedure. After removal of ether by evaporation from the ether-treated extracts and of the aqueous phases from the DOC-extracted specimens, the homogenates were clarified by centrifugation at 100,000 × *g* for 40 min at 5°C. Supernatants were then concentrated on the Diaflo UM-10 membrane (Aminco Corp.). The immunodiffusion assays were performed on microslides using 0.8% agarose. Patterns were cut using the LKB apparatus.

Antiserum to gs antigen: The antisera used for most of the CF tests for gs antigen in embryos were made in inbred Fisher rats carrying transplanted Moloney sarcoma virus (MSV) induced tumors which characteristically contained large amounts of murine gs antigen. In order to ensure optimum sensitivity, only those sera were selected for pooling which had titers of 1:160 or higher when tested with various standard gs antigen-containing infected tissue cultures, and with several rat and mouse tumor tissues also containing antigens;[46] several normal cell cultures and tissue antigens were also used for screening the sera for nonspecific reactions prior to pooling. A requirement for preparation of the antiserum pools used in these studies was that the sera included in the pools should have antibody titers of 1:160 or higher when tested with 10% antigen extracts of spleens from newborn NIH Swiss mice.[51] The 10% extract antigens made from embryonic and newborn tissue antigens were routinely screened at 1:2 and 1:4 dilutions with 8 units of the high titered rat sera. Many of the embryonic antigens were also tested in CF and in gel diffusion with 4 units of hyperimmune antisera made by injecting guinea pigs into the footpad twice at 10-day intervals with purified gs antigens together with Freund's adjuvants;[41] four additional injections of antigen were made without adjuvant, also at 10-day intervals. The antisera obtained was highly specific for the gs antigen, having no reaction in CF or gel diffusion with normal cell antigens or with intact virions.

Results. Whole NIH Swiss embryos taken at 10, 12, and 14 days after insemination, and spleens, thymuses, and livers of older (16–19 day) embryos, revealed complement-fixing antigens with high frequency (Table 1). Most of the spleen, thymus, and liver specimens from 18-day-old embryos, newborns, and weanlings were also positive, although fewer reactions occurred in

TABLE 1. *Complement-fixing antigen in embryonic and newborn tissues of NIH Swiss mice.*

	Whole embryo	Spleen	Thymus	Liver
10-day embryo	47/47*	—	—	—
12-day embryo	30/30	—	—	—
14-day embryo	55/61	—	—	—
18-day embryo	—	7/11	11/11	9/10
Newborn	—	10/11	11/11	5/10
Weanling, 30 days	—	59/60	19/20	NT†

* Number positive at a dilution of 1:2 (1:20 or higher actual dilution of tissue)/number of specimens tested.

† NT = not tested.

the newborn livers. Table 2 shows the actual titers of the antigens detected in extracts of pooled spleens, thymuses, and livers of 18-day-old NIH Swiss embryos together with titers on the same tissues in their mothers.

The gs antigens of the embryonic and newborn spleens and thymuses were not sedimentable at 58,000 *g*-hr and were resistant to ether (Table 3). The antigens were reactive at low dilutions with guinea pig sera as well as with the standard rat-MSV antisera.

TABLE 2. *CF antigen titer in pooled tissue extracts (10%) from 18-day NIH Swiss embryos.*

	Spleen	Thymus	Liver
Mother no. 1	<4*	8	NT†
Pool, 10 fetuses	4	>8	2
Mother no. 2	2	4	NT
Pool, 9 fetuses	<2	>8	>8
Mother no. 3	<2	8	NT
Pool, 10 fetuses	<2	8	<2
Mother no. 4	>8	2	NT
Pool, 9 fetuses	8	>8	4
Mother no. 5	>8	4	NT
Pool, 10 fetuses	4	>8	4
Mother no. 6	2	2	4
Pool, 10 fetuses	4	>8	>8

* Reciprocal of dilution.
† NT = not tested.

TABLE 3. *CF reactivity of NIH Swiss newborn extracts (10%) after ether treatment and sedimentation.**

Spleen and thymus (untreated)	MSV 18†	Gp Sera 26116‡
Clarified extract	>4	2
Upper supernate	>4	2
Lower supernate	>4	2
Pellet	<2	<2
Spleen and thymus (ether Rx)	**MSV 18†**	**Gp Sera 26116‡**
Clarified extract	>4	2
Upper supernate	>4	2
Lower supernate	>4	2
Pellet	<2	<2

* 58,000 g for 1 hr.
† MSV 18 = rat antisera containing antibodies to gs and envelope antigen.
‡ Guinea pig sera to gs antigen only.

TABLE 4. *Murine C-type virus group-specfic antigen in NIH Swiss embryos by immunodiffusion and complement-fixation.*

Age of embryo	MSV rat 18	Guinea-pig anti-gs	Gel diffusion*
11–12 day	4†	2	±
13–14 day	16	8	+
18–19 day spleen	8	8	+
18–19 day thymus	16	8	+
18–19 day liver	16	16	+
Newborn spleen	8	8	+
Newborn thymus	32	8	+
Newborn liver	32	16	+

* + = reaction of identity with purified virion gs antigen using both rat and guinea pig antiserum.
† CF titer reciprocal (20% homogenates treated with deoxycholate–genetron or Tween 80–ether, then concentrated 10-fold using Diaflo membrane).

Despite many hundreds of attempts, infectious RNA tumor viruses have never been isolated from tissue extracts and cell cultures of normal NIH Swiss mice,[46,52] yet gs antigen appears to be expressed in relatively high titers in virtually all normal postnatal hematopoietic tissues, as well as in embryos. Because of our total inability to isolate virus from NIH Swiss tissues, precise identification of the putative reactive gs antigen was absolutely essential. In Table 4 it is shown that positive reactions in gel diffusion were correlated with

those obtained in CF; also the antigens reacted not only with the standard rat sera but also with the guinea pig sera made with electrofocused highly purified antigens.[41] Fig. 1, a typical protocol, clearly indicates that the gs antigens

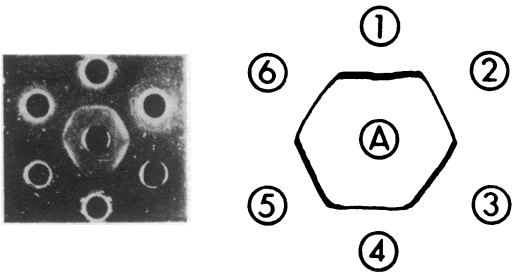

FIG. 1. Immunodiffusion assays of embryonic NIH Swiss mouse tissues. *Center well A:* MSV rat 18; *Wells 1, 3, 5*—purified gs antigen; *2*—newborn thymus; *4*—18-day embryo thymus; and *6*—18-day embryo liver.

present in 18-day-old embryo thymus and liver tissues have lines of identity with the purified gs antigen as well as with the gs antigen present in the newborn thymus. In other tests,[53] similar lines of identity were also established between these antigens and gs antigens demonstrated in subcutaneous sarcomas induced by 3MC in NIH Swiss, BALB/c/Cr, AKR, and CF1 strains of mice, and with antigens present in spleens and thymuses of the mothers of the embryos.

Group-specific gs antigens were also demonstrated in embryos and newborns of 10 additional strains of mice; the findings on 7 strains are shown in Table 5. Each of the laboratory strains shown have been characterized as low leukemia strains and all but the CF1 strain have been found devoid of infectious virus in the COMUL test. When tested for virus as embryos, newborns or young adults,[46,54] the BALB/c, C57B1, and C3H/Bi strains rarely yielded virus except in old age or when lymphomas or sarcomas were induced by radiation or chemicals.[14,55,56] Wild (feral) mice trapped in rural areas on the East and West Coasts of the United States, like the NIH Swiss have not yielded infectious RNA tumor viruses, despite numerous attempts; chemical and radiation-induced tumors were also negative for virus, but tumors were frequently positive for gs antigen and occasionally showed C-type particles when viewed by electron microscopy.[19] Examination of individual tissue responses in the experiments summarized in Table 5 revealed that with the exception of several CF1 embryos, all of the embryos were positive in one tissue or another.

Subsequent tests of 10-, 14-, and 18-day-old embryos from a special inbred "pedigreed" strain of BALB/c/Cr were virtually negative for gs antigen.[17] Moreover, hematopoietic organs of the pedigreed strain were found to be almost completely switched off for early postnatal expression of gs antigen. It was quite surprising, therefore, to discover that pools of embryos from BALB/c mothers of the pedigreed strain taken 6 days after insemination were as strongly positive as the NIH Swiss embryos, often giving titers of 1:8 or higher, whereas many embryos 10–13 days in term and tissues from other older embryos and newborns gave only negative reactions at a 1:2 dilution. It now appears that in this strain the gs antigen expression which is high in the undifferentiated 6-day-old embryo becomes subject to relatively strong repressor action during the

TABLE 5. *CF (gs) antigen in embryos and newborns—tissue pools of various strains.*

		Embryos					Newborns			
Age	Strain	No.	Spleen	Thymus	Liver	Whole embryo	No.	Spleen	Thymus	Liver
18 day	C3H/bi (*H-2^k*)	39*	5/5	5/5†	5/5	—	20*	3/5	5/5	4/4
18 day	BALB/c/Cr (*H-2^d*)	46	2/4	5/5	5/5	—	29	4/5	5/5	4/5
18 day	BALB/c/An (*H2^d*)	23	2/3	3/3	2/3	—	50	8/8	8/8	6/8
13–19 day	C57B1/J (*H-2^b*)	33	1/2	2/2	2/2	6/6	8	0/2	1/2	2/2
18 day	CF1 (NI)‡	56	0/7	4/7	4/7	—	43	5/7	6/7	2/2
16–18 day	Wild (feral)	18	2/3	3/3	2/2	17/19	5	1/1	1/1	ac
	Positive/Totals		12/24	22/25	20/24	23/25		21/28	26/28	18/21

* Number of embryos or newborns included in the designated pools.
† Number of pools from different mothers, positive/total; positive = >20 dilution w/v of tissue.
‡ NI = not inbred.

middle and late embryonic development, a switched off state which, as determined from other studies, persists postnatally for several months; after 6 months, the gs antigen appears in the spleen with increasing frequency with increasing age; later in life, the antigen is found in a high proportion of tumors.[17]

Perhaps of special interest was the detection of gs antigen in most embryonic and several newborn tissues of wild *Mus musculus*. Large scale surveys of wild mice trapped in Maryland and Los Angeles revealed that less than 2% of young adult and older animals had demonstrable gs antigen levels in their normal spleens and thymuses; gs antigen, however, was demonstrated in wild mice later in life, particularly in subcutaneous sarcomas produced by 3-methylcholanthrene.[19] In most of the strains of mice, additional embryonic and newborn data besides that shown in Table 1 indicate that gs antigen expressions may occur more frequently and in higher titer in the younger embryos.

It is important to note at this point that "positive" and "negative" reactions at low dilutions in the CF test are not "absolutes" but most probably represent differing levels of reaction fluctuating around a threshold level. Comparisons of the relative sensitivities of fluorescent antibody and complement-fixation tests indicate that 10–50% of the cells in a culture preparation usually show specific fluorescence, when the same extracts show a reaction at a 1:2 dilution in the complement fixation test.[57] Obviously, therefore, a negative or partial complement-fixing reaction at a 1:2 dilution cannot be regarded as evidence for total absence of the gs antigen. Clearly, future studies utilizing tests providing more sensitive and quantitative assays of gs antigen are indicated. Tests such as fluorescent antibody procedure will be useful for the purpose of charting localized expressions in various developing organs and the sequential switching on and off of the antigen in different tissues at different periods of em-

bryo development. For instance, muscle, subcutaneous, and certain other mesenchymal tissues which are regularly negative for complement-fixing antigen postnatally are also generally negative in embryos and newborns, becoming positive only when sarcomas occur spontaneously or are induced with carcinogenic chemicals.[2,14,17]

Electron microscopy studies of embryos are still incomplete. It is apparent, however, that embryo tissues having high gs antigen titers frequently show clear-cut evidence of C-type particles, some budding from the cell membrane. For instance, NIH Swiss mouse embryos at 14 and 18 days reveal C-type particles more frequently than the other strains; the significance of these particles in tissues is unknown since hundreds of attempts, *in vitro* and *in vivo*, to recover infectious virus from NIH Swiss mice and their embryos by several laboratories have failed.

Discussion. Dougherty *et al.*[48] and subsequently Sarma *et al.*[67] reported gs antigens of the avian RNA tumor viruses and C-type particles in the livers of certain "avian leukosis free" chick embryos; very little correlation between particles and antigen was noted. Payne and Chubb[21] carried the observation further by showing that the gs antigen expression in one of two inbred lines of chickens was probably dependent on a Mendelian dominant gene. Meier *et al.*[22] recently identified a similar dominant gene determinant of the murine gs antigen. The high incidence of gs antigen in embryos of many strains of mice (including feral mice) described in this communication suggests that this interesting gene expression may be universal in mouse embryos and therefore very likely to have considerable importance in embryogenesis. As mentioned earlier (see above) the immunological tolerance to gs antigens demonstrated in hamsters and cats as well as in mice and chickens increases the likelihood that the RNA virus genomes may have an important role to play in vertebrate embryogenesis.[3]

The unique RNA-dependent DNA polymerase recently discovered in the avian and murine C-type RNA tumor viruses[58,59] (an observation extended to hamster, cat and viper RNA tumor viruses and in murine B-type mammary tumor virus by a number of investigators[60–63]) undoubtedly represents a major step toward explaining the mechanisms involved in the gene activity of RNA tumor viruses. Should the endogenous RNA virus genome also be found to synthesize DNA, which seems very likely, these findings in the embryo will become doubly interesting. However, whether or not the gs antigen expressions are eventually shown to serve biologically useful functions in embryogenesis, its value as a marker for specific genome activity in embryonic cells and in postnatal hematopoietic tissues and tumors seems obvious.

Some of the basic activities of the C-type RNA genome might turn out to be essentially similar in embryonic development and in tumorigenesis; for instance, should it carry a message to replicate, it could conceivably be useful during the well regulated period of embryogenesis, while derepression in differentiated cells later in life leading also to cell replication could prove disastrous. Although an oversimplified concept such as this has little value as it stands, it could lead to more intensive search for functional activity on the part of easily assayed gene expressions found in embryo and tumor cells; their possible importance in cer-

tain normal tissues subject to continuous or recurrent replication such as the hematopoietic system and the reproductive organs should also be explored.[64]

Abbreviations: gs, group-specific; CF, complement fixation.

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