Brief Definitive Report

INFLUENCE OF *Fv-1* ALLELES ON CELLULAR EXPRESSION OF gp70*

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Variants of gp70 (glycoprotein-70), which is the major envelope protein of C-type mouse virus and is also expressed on plasma membranes, can be identified immunogenetically by the type-specific antigens Gix and Ec. (Ec is the type-antigen of a species of gp70 formerly designated X-gp70 [1, 2].) Gix antigen occurs on cells of normal mice that are not overt producers of virus, and its expression is then governed by two unlinked mendelian genes, *Gv-1* and *Gv-2* (3). In contrast, Ec^+ gp70 has been found only in virus-producing mice (2), suggesting that its expression may be associated with production of virus or by genes that influence the production of virus. Accordingly we investigated whether expression of Ec^+ gp70 by thymocytes of AKR mice depends on alleles at the *Fv-1* locus which control the replication of N-tropic and B-tropic virus (4).

Thymocytes of various inbred, congenic and hybrid mice were typed for presence or absence of Ec^+ gp70 by gel electrophoresis of material precipitated by anti-X.1 serum (5), which recognizes exclusively Ec^+ gp70 (2), from lysates of ^{125}I-labeled thymocytes. The results, summarized in Table I and illustrated in Fig. 1, indicate that expression of Ec^+ gp70 on thymocytes requires the $Fv\text{-}1^n$ allele, which is permissive for replication of N-tropic virus.

The salient findings are as follows: (*a*) The thymocytes of AKR and of congenic AKR-$H\text{-}2^b$ mice, both $Fv\text{-}1^n$, express Ec^+ gp70 (Fig. 1, tracks 2 and 4), whereas the thymocytes of AKR-$Fv\text{-}1^b$ and AKR-$H\text{-}2^b$:$Fv\text{-}1^b$ do not (Fig. 1, tracks 6 and 8); thus substitution of the allele $Fv\text{-}1^b$ for $Fv\text{-}1^n$ in AKR mice suppresses Ec^+ gp70. (*b*) The thymocytes of AKR-$H\text{-}2^b$ mice express Ec^+ gp70 (Fig. 1, track 4), whereas the thymocytes of AKR-$H\text{-}2^b$:$Fv\text{-}1^b$ do not (Fig. 1, track 8); thus substitution of the allele $H\text{-}2^b$ for $H\text{-}2^k$ in AKR mice, although it greatly delays the onset of leukemia (7), does not demonstrably affect expression of Ec^+ gp70. (*c*) The hybrid mouse (B6-$Fv\text{-}1^n$ × AKR)F_1, genotype $Fv\text{-}1^n/Fv\text{-}1^n$, expresses Ec^+ gp70 (Fig. 1, track 10), whereas the congenic hybrid mouse (B6 × AKR)F_1, genotype $Fv\text{-}1^b/Fv\text{-}1^n$, does not (Fig. 1, track 12); this is in accord with the dominance of $Fv\text{-}1^b$ for suppressed replication of N-tropic virus (4). (*d*) Neither B6 mice (genotype $Fv\text{-}1^b$) nor B6-$Fv\text{-}1^n$ congenic mice express Ec^+ gp70 (Fig. 1, tracks 14 and 16); thus $Fv\text{-}1^n$ is not the structural gene for Ec^+ gp70, and the action of $Fv\text{-}1^n$ in permitting expression of this gp70 species in AKR mice evidently depends on the same mechanism that facilitates replication of N-tropic virus of the type ascribed to the loci *Akv-1* and *Akv-2* (8–10). (*e*) The congenic mouse strain C57L-Akvp, Gix^+:$Fv\text{-}1^n$ (11), and strain 129, Gix^+:$Fv\text{-}1^{nr}$, do not express

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TABLE I

Ec^+ gp70 Phenotypes of Thymocytes of Various Inbred and Hybrid Mice‡*

Genetic background	Ec^+ gp70 phenotypes of thymocytes			
	Positive	Number of mice tested§	Negative	Number of mice tested§
AKR (*Fv-1^n*)	AKR	10	AKR-*Fv-1^b*	3
	AKR-*H-2^b*	3	AKR-*H-2^b:Fv-1^b*	3
B6 (*Fv-1^b*)			B6	12
			B6-*Fv-1^n*	5
Hybrid (F_1)	B6-*Fv-1^n* × AKR (*Fv-1^n/Fv-1^n*)	3	B6 × AKR (*Fv-1^b/Fv-1^n*)	3
Other			C57L-Akvp	4
			129	11

* See Fig. 1: based on presence or absence of a band in the position characteristic of gp70 in sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) of material precipitated from lysed ^{125}I-labeled thymocytes by anti-X.1 serum. Anti-X.1 serum, which recognizes the antigen now called Ec, is made by immunizing (BALB/c × B6)F_1 hybrid mice with the leukemia BALB.RLƟ1 (5).

‡ Aged 6–8 wk; the AKR-*Fv-1^b* and AKR-*H-2^b:Fv-1^b* groups included also mice up to 9 mo of age, at which time the thymocytes still did not express Ec^+ gp70.

§ Each test performed with a single thymus.

Ec^+ gp70 (Fig. 1, tracks 18 and 20); this further indicates that expression of Ec^+ gp70 depends on conjunction of *Fv-1^n* with loci of the *Akv-1* and *Akv-2* type that are associated with high output of virus.

In addition to the data for precipitations with anti-X.1 serum, Fig. 1 includes results with goat antiserum to gp70 of Rauscher-MuLV (odd numbered tracks). This group-specific anti-gp70 serum precipitates gp70 from AKR-*Fv-1^b* and from AKR-*H-2^b:Fv-1^b* thymocytes (Fig. 1, tracks 5 and 7); the lesser density of these bands in comparison with AKR and AKR-*H-2^b* (Fig. 1, tracks 1 and 3) can be explained by absence of Ec^+ gp70, the residual bands being composed of other gp70 type-variants.

It would certainly be helpful to know whether mouse strains in which Ec^+ gp70 is expressed differ from strains in which Ec^+ gp70 is unexpressed or suppressed (Table I) in respect to the susceptibility to the spontaneous or induced leukemogenesis, but this question has not yet been sufficiently studied.

Summary

Type-variants of gp70 (glycoprotein-70), which is the major envelope protein of C-type mouse virus and is also found in plasma membranes, are identified immunogenetically by the antigens Gix and Ec. Cellular expression of Gix^+ gp70 does not depend on production of virus, but expression of Ec^+ gp70 (formerly X-gp70) has been observed only in AKR and other strains of mice that produce large amounts of virus throughout life. To test the inference that cellular expression of Ec^+ gp70 is secondary to production of virus we examined the effect of *Fv-1* alleles, which govern the replicability of N-tropic and B-tropic C-type virus, on the expression of Ec^+ gp70 on thymocytes. By typing thymocytes of *Fv-1*-congenic mice for Ec^+ gp70 we found that manifestation of the Ec^+ gp70 phenotype requires the *Fv-1^n* allele, which is permissive for replication of N-tropic virus produced by AKR and other virus-producing mouse strains. Substitution of the *Fv-1^b* allele for the *Fv-1^n* allele abolishes demonstrable expression of Ec^+ gp70 by AKR thymocytes at ages up to 9 mo, the oldest AKR mice tested.

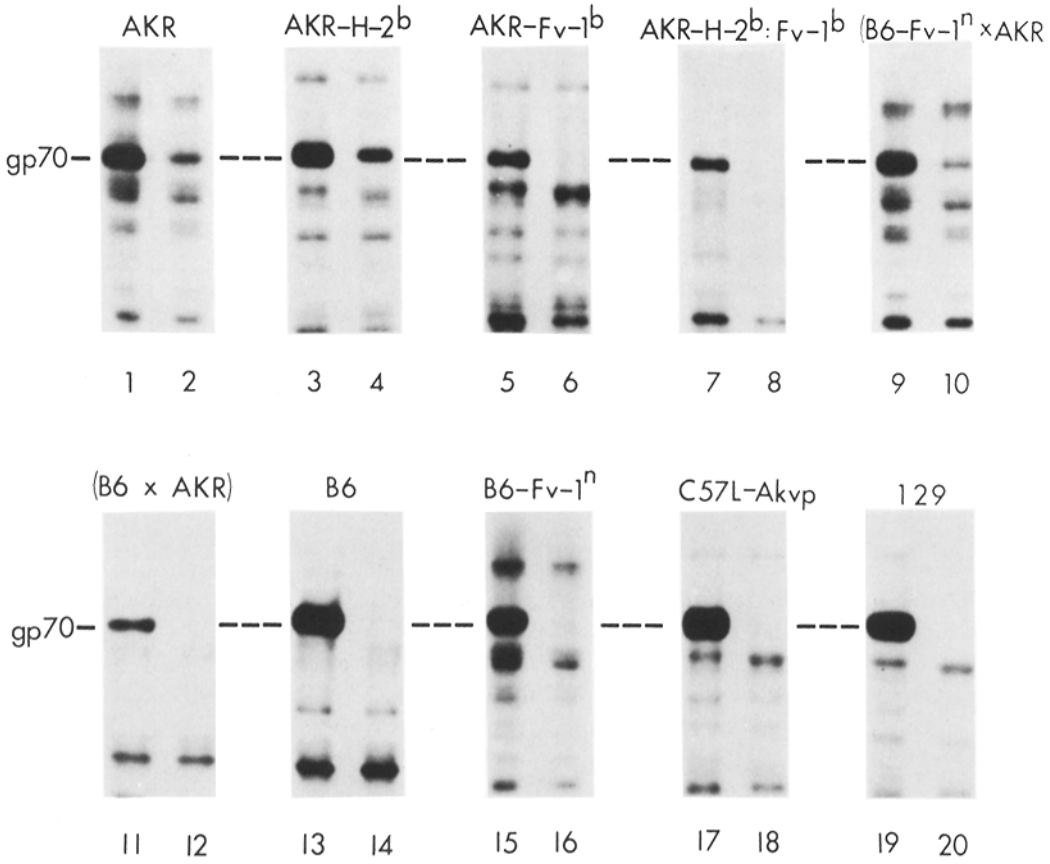

FIG. 1. SDS-PAGE of material precipitated from ^{125}I-labeled thymocyte lysates by group-specific goat anti-Rauscher-MuLV-gp70 serum (first of each pair of tracks; odd numbers) and by the type-specific antiserum anti-X.1 (second of each pair of tracks, even numbers). The method of the SDS-PAGE was as described (6) except for substitution of *Staphylococcus aureus* (Pansorbin; Calbiochem-Behring Corp., American Hoechst Corp., San Diego, Calif.) for anti-Ig. Each pair of tracks relates to a single thymus; the numbers of mice tested, of the genotypes indicated, are shown in Table I.

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