In some areas of rat cerebrum AChE can be used to identify cholinergic neurons; in most areas its presence is not sufficient to identify a neuron as capable of releasing acetylcholine at its axon terminals (*33*). AChE may therefore be present in some noncholinergic neurons, and ChAT is a more specific marker for cholinergic neurons. Nevertheless, the presence of AChE as a neuronal marker should be of value in itself. For example, AChE in the absence of ChAT could signify a neuron postsynaptic to a cholinergic neuron. In this case, the coexistence of AChE and SOM could indicate that cortical somatostatinergic neurons are innervated by cholinergic neurons, with the deficiencies seen in AD/SDAT reflecting loss of both the presynaptic and postsynaptic elements. Acetylcholine has been shown to stimulate the neuronal release of SOM in similar cultures of rat cerebral cortex (*23*). Although muscarinic cholinergic receptors are not reduced in the cortex of patients with AD (*34, 35*), those receptors present on the relatively small population of somatostatinergic neurons could represent only a small fraction of the total number of muscarinic receptors.

In summary, we have demonstrated the coexistence of AChE and SOM-LI in neurons derived from mammalian cerebral hemispheres. As far as we are aware, these findings constitute the first neuroanatomical association of a cholinergic marker and SOM within mammalian central nervous system neurons. The absence of a demonstrable coexistence of AChE and CCK-8-LI suggests some specificity for the relationship between AChE and SOM-LI. The most immediate importance of these findings is in relation to the known diminution of both cholinergic innervation and of SOM levels of brains of persons affected by AD/SDAT. It is not known if SOM and AChE also coexist in cerebral neurons in vivo, or if AChE in these neurons represents a cholinergic neuron or a neuron receiving cholinergic input. The implications of the coexistence of AChE and SOM-LI in the same cerebral neurons are that these systems may be both anatomically and physiologically linked, and that this association may be important in understanding the pathophysiology of processes such as AD/SDAT and the functioning of the normal brain.

JOHN R. DELFS*
CHUN-HAN ZHU
MARC A. DICHTER
Department of Neurology, Harvard Medical School and *Division of Neuroscience, Children's Hospital, Boston, Massachusetts 02115*

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* To whom all correspondence should be addressed.

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Gene Product of v-*fgr onc*: Hybrid Protein Containing a Portion of Actin and a Tyrosine-Specific Protein Kinase

Abstract. *The nucleotide sequence of the region of Gardner-Rasheed feline sarcoma virus (GR-FeSV) encoding its primary translation product, p70$^{gag\text{-}fgr}$, has been determined. From the nucleotide sequence, the amino acid sequence of this transforming protein was deduced. Computer analysis indicates that a portion of P70$^{gag\text{-}fgr}$ has extensive amino acid sequence homology with actin, a eukaryotic cytoskeletal protein. A second region of P70$^{gag\text{-}fgr}$ is closely related to the tyrosine-specific kinase gene family. Thus, the v-*fgr oncogene appears to have arisen as a result of recombinational events involving two distinct cellular genes, one coding for a structural protein and the other for a protein kinase.*

Gardner-Rasheed feline sarcoma virus (GR-FeSV) is a replication-defective, acute transforming retrovirus that was isolated from a cat fibrosarcoma (*1*). This virus arose by recombination of the nondefective helper feline leukemia virus (FeLV) and cellular sequences present within the normal cat genome (*2*). Analysis of a DNA clone containing the proviral genome of GR-FeSV revealed the presence of 1.7 kilobase pairs (kbp) of cell-derived sequences that are flanked by a partial *gag* gene at the 5′ end and partial *env* gene at the 3′ end (*2*). These cell-derived sequences, termed v-*fgr*, appear to code for the oncogenic potential of the viral genome. Cells transformed by GR-FeSV express a 70,000-dalton protein, which is recognized by antibodies to the helper virus structural protein p15 but not by antibodies to other helper virus proteins (*2, 3*). Thus the primary translational product of GR-FeSV, called P70$^{gag\text{-}fgr}$, is a hybrid molecule, containing at least a portion of FeLV p15 as well as FeLV-unrelated component coded by v-*fgr* sequences (*2, 3*). The hybrid P70$^{gag\text{-}fgr}$ has a closely associated kinase activity with specificity for tyrosine residues (*3*). In an effort to understand the mechanism of action of the v-*fgr* oncogene and its relationship to other cell-derived genes, we have undertaken primary DNA sequence analysis of the region of GR-FeSV encoding P70$^{gag\text{-}fgr}$ (*1*). The nucleotide sequence of the entire region coding for the P70$^{gag\text{-}fgr}$, as determined by the procedures of Maxam and Gilbert (*4*), is shown in Fig. 1.

*The v-*fgr *nucleotide sequence.* Since the v-*fgr onc* gene product contains *gag*-gene determinants, we compared the sequence in Fig. 1 with that of the Snyder-Theilen feline sarcoma virus *gag*-gene

(5). Such a comparison revealed extensive nucleic acid and protein sequence homology between the two genes from nucleotide 1 to nucleotide 354. Downstream of this position, no sequence homology was observed between the two viral genes, thus localizing the point of recombination between the helper viral *gag* and cell-derived sequences. Beyond this point of recombination in GR-FeSV, the open reading frame extended for an additional stretch of 1635 bases terminating with a TAA codon. This open reading frame has the coding capacity for a polypeptide of 663 amino acids having a molecular size of 70,000 daltons. This is in good agreement with that observed for the *gag-fgr* hybrid protein synthesized by GR-FeSV transformed cells. These results demonstrate the P70$^{gag\text{-}fgr}$ protein consists of 118 amino acids of FeLV p15 region followed by 540 amino acids that are specific to the v-*fgr* region. In order to determine the 3′ v-*fgr* helper virus junction, we compared the nucleotide sequence shown in Fig. 1 with that of the FeLV envelope gene (6). This compari-

```
                                        30                                                  60                                                  90
ATG GGC CAA ACT ATA ACT ACC CCC TTA AGC CTC ACC CTT GAT CAC TGG TCT GAA GTC CGA GCA CGG GCC CAT AAT CAA GGT GTC GAG GTC
Met Gly Gln Thr Ile Thr Thr Pro Leu Ser Leu Thr Leu Glu His Trp Ser Glu Val Arg Ala Arg Ala His Asn Gln Gly Val Glu Val (30)
                                       120                                                 150                                                 180
CGG AAA AAG AAA TGG ATT ACC TTA TGT GAG GCC GAA TGG GTG ATG ATG AAT GTG GGC TGG CCC CGA GAA GGA ACT TTT TCT CTT GAT AAC
Arg Lys Lys Lys Trp Ile Thr Leu Cys Glu Ala Glu Trp Val Met Met Asn Val Gly Trp Pro Arg Glu Gly Thr Phe Ser Leu Asp Asn (60)
                                  ▼ Bgl II  210  ▼ Sma I                                   240                                                 270
ATT TCC CAG GTT GAA AAA AAG ATC TTC GCC CCG GGA CCG TAT GGA CAC CCC GAC CAA GTT CCT TAC ATT ACC ACA TGG AGA TCC TTA GCC
Ile Ser Gln Val Glu Lys Lys Ile Phe Ala Pro Gly Pro Tyr Gly His Pro Asp Gln Val Pro Tyr Ile Thr Thr Trp Arg Ser Leu Ala (90)
                                       300                                                 330    v-fgr-helper viral junction▼  360
ACA GAC CCC CCT TCG TGG GTT CGT CCG TTC CTA CCC CCT CCC AAA CCT CCC ACA TCC CTC CCT CAA CCT CAC TCG CCG CAG CCG GCC CGT
Thr Asp Pro Pro Ser Trp Val Arg Pro Phe Leu Pro Pro Pro Lys Pro Pro Thr Ser Leu Pro Gln Pro His Ser Pro Gln Pro Ala Arg (120)
                                       390                                                 420                                                 450
GCT CTG TGT CGT CCC GCC GTT TGT CGT CCG CGT CCA CTG CCG CCA CTT CCA CCG ACC GCA ATG GAA GAG GAG GTC GCC GCG CTG GTC ATC
Ala Leu Cys Arg Pro Ala Val Cys Arg Pro Arg Pro Leu Pro Pro Leu Pro Pro Thr Ala Met Glu Glu Glu Val Ala Ala Leu Val Ile (150)
                                       480                                                 510                                                 540
GAC AAT GGC TCT GGC ATG TGC AAG GCG GGC TTT GCT GGG GAC GAC GCC CCC CGA GCC GTG TTC CCG TCC ATC GTC GGG CGG CCC CGG CAC
Asp Asn Gly Ser Gly Met Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe Pro Ser Ile Val Gly Arg Pro Arg His (180)
                                       570                                                 600                                                 630
CAG GGC GTT ATG GTG GGC ATG GGC CAG AAG GAC TCC TAC GTG GGC GAC GAG GCC CAG AGC AAG CGG GGC ATC CTG ACC CTC AAG TAC CCC
Gln Gly Val Met Val Gly Met Gly Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly Ile Leu Thr Leu Lys Tyr Pro (210)
                                       660          ▼ Bgl II                               690                                                 720
ATC GAA CAC GGC ATT GTC ACC AAC TGG GAC GAC ATG GAG AAG ATC TGG CAC CAC ACC TTC TAC AAC GAG CTG CGC GTG GCC CCC GAG GAG
Ile Glu His Gly Ile Val Thr Asn Trp Asp Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val Ala Pro Glu Glu (240)
                                       750                                                 780                                                 810
CAC CCG GTG CTG CTC ACC GAG GCC CCC TTG AAC CCC AAG GCC AAC CGT GAG AAG ATG ACT CAG ATC ATG TTC GAG ACC TTC AAC ATT CCC
His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn Ile Pro (270)
                                       840                                                 870                                  Pvu II ▼       900
AGC AAC TAC GTG GCC CCT GTG GAC TCC ATC CAG GCT GAA GAG TGG TAC TTT GGA AAG ATT GGG AGG AAG GAT GCG GAG AGG CAG CTG CTC
Ser Asn Tyr Val Ala Pro Val Asp Ser Ile Gln Ala Glu Glu Trp Tyr Phe Gly Lys Ile Gly Arg Lys Asp Ala Glu Arg Gln Leu Leu (300)
                     ▼ Sma I           930                                                 960                                                 990
TCC CCA GGG AAC GCC CGG GGG GCC TTC CTC GTT CGT GAG AGT GAG ACT ACC AAA GGT GCC TAC TCC CTG TCC ATC CGA GAT TGG GAC GAG
Ser Pro Gly Asn Ala Arg Gly Ala Phe Leu Val Arg Glu Ser Glu Thr Thr Lys Gly Ala Tyr Ser Leu Ser Ile Arg Asp Trp Asp Glu (330)
                                      1020                                                1050                                                1080
GCC AGA GGC GAC CAT GTG AAG CAT TAC AAA ATC CGC AAG CTG GAC ACG GGT GGC TAT TAC ATC ACC ACA CGG GCC CAG TTC AAC TCA GTG
Ala Arg Gly Asp His Val Lys His Tyr Lys Ile Arg Lys Leu Asp Thr Gly Gly Tyr Tyr Ile Thr Thr Arg Ala Gln Phe Asn Ser Val (360)
                                      1110                                                1140                                                1170
CAG GAG CTG GTG CAG CAC TAC GTT GAG GTG AAC GAT GGG CTA TGC CAC CTG CTC ACA GCG GCC TGC ACC ACC ATG AAG CCG CAG ACA ATG
Gln Glu Leu Val Gln His Tyr Val Glu Val Asn Asp Gly Leu Cys His Leu Leu Thr Ala Ala Cys Thr Thr Met Lys Pro Gln Thr Met (390)
                                      1200                                                1230                                                1260
GGC CTG GCC AAG GAC GCC TGG GAG ATC AGC CGC AGC TCC ATC ACG CTC CAG CGC CGG CTA GGC ACC GGC TGC TTC GGA GAC GTG TGG CTG
Gly Leu Ala Lys Asp Ala Trp Glu Ile Ser Arg Ser Ser Ile Thr Leu Gln Arg Arg Leu Gly Thr Gly Cys Phe Gly Asp Val Trp Leu (420)
                                      1290                                                1320                                                1350
GGC ATG TGG AAT GGC AGC ACG AAG GTG GCG GTG AAG ACG CTG AAG CCG GGA ACC ATG TCC CCG AAG GCC TCC CTG GAG GAG GCG CAG ATC
Gly Met Trp Asn Gly Ser Thr Lys Val Ala Val Lys Thr Leu Lys Pro Gly Thr Met Ser Pro Lys Ala Ser Leu Glu Glu Ala Gln Ile (450)
                                      1380     ▼ Pvu II                                   1410                                                1440
ATG AAG CTG CTG CGG CAC GAC AAG CTG GTG CAG CTG TAC GCC GTG GTG CCG GAG GAG CCC ATC TAC ATC GTG ACA GAG TTC ATG TGC CAC
Met Lys Leu Leu Arg His Asp Lys Leu Val Gln Leu Tyr Ala Val Val Pro Glu Glu Pro Ile Tyr Ile Val Thr Glu Phe Met Cys His (480)
                                      1470                                                1500                                                1530
GGT AGC TTG CTG GAG TTC CTC AAG GAC CAG GAG GGC CAG GAT TTG ACA CTG CCC CAG TTG GTG GAC ATG GCA GCC CAG GTA GCT GAG GGC
Gly Ser Leu Leu Glu Phe Leu Lys Asp Gln Glu Gly Gln Asp Leu Thr Leu Pro Gln Leu Val Asp Met Ala Ala Gln Val Ala Glu Gly (510)
                                      1560                                                1590                                                1620
ATG GCC TAC ATG GAG CGC ATG GAC TAT ATC CAC CGC GAC CTG AGG GCA GCC AAC ATC CTT GTT GGG GAA CGG CTG GTG TGC AAG ATC GCT
Met Ala Tyr Met Glu Arg Met Asp Tyr Ile His Arg Asp Leu Arg Ala Ala Asn Ile Leu Val Gly Glu Arg Leu Val Cys Lys Ile Ala (540)
                                      1650                                                1680                                                1710
GAC TTC GGG CTG GCC CGT CTC ATT GAG GAT AAT GAG TAC AAC CCC CGG CAA GGG GCC AAG TTC CCT ATC AAG TGG ACA GCC CCA GAG GCT
Asp Phe Gly Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr Asn Pro Arg Gln Gly Ala Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala (570)
                                      1740                          ▼ Bam HI     1770                                                1800
GCT CTC TTT GGC AGA TTC ACC ATC AAG TCA GAT GTG TGG TCC TTT GGG ATC CTG CTC ACT GAA CTC ATC AGC AAG GGC CGA GTT CCC TAC
Ala Leu Phe Gly Arg Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Thr Glu Leu Ile Ser Lys Gly Arg Val Pro Tyr (600)
                                      1830                          ▼ Kpn I     1860                                                1890
CCA GGC ATG AAT AAC CGG GAA GTG TTG GAA CAG GTG GAG CAT GGG TAC CAC ATG CCA TGC CCT CCG GGC TGC CCA GCG TCC CTG TAC GAG
Pro Gly Met Asn Asn Arg Glu Val Leu Glu Gln Val Glu His Gly Tyr His Met Pro Cys Pro Pro Gly Cys Pro Ala Ser Leu Tyr Glu (630)
                                      1920                                 Pst I ▼     v-fgr-helper viral junction ▼ 1980
GCC ATG GAG CAG ACC TGG CGT CTG GAC CCA GAG GAG AGG CCT ACC TTC GAG TAC CTG CAG TCC TTC CTT GAG GAC TAC TTC AAC GGA CCC
Ala Met Glu Gln Thr Trp Arg Leu Asp Pro Glu Glu Arg Pro Thr Phe Glu Tyr Leu Gln Ser Phe Leu Glu Asp Tyr Phe Asn Gly Pro (660)
                                      2010
CAA CAG AAC TAA AGA CTG TTG GCT CTG CCT GGT TTC TCG ACC ACC
Gln Gln Asn ***
```

Fig. 1. Nucleotide sequence of GR-FeSV proviral genome coding for *gag-fgr* polyprotein. The sequence proceeding in the 5′ to 3′ direction has the same polarity as GR-FeSV genomic RNA. Position 1 corresponds to the ATG codon at the amino terminus of the *gag* gene. The amino acid sequence deduced from the open reading frame is given below the nucleotide sequence. Bracketed numbers at the end of each line indicate the amino acid positions. Cleavage sites for some of the important restriction enzymes are also indicated. Termination codon is designated by ***.

son revealed that the two sequences are identical beyond position 1976. Thus the recombination at the 3′ end occurred within the envelope gene, altering the reading frame which created the terminator codon for P70$^{gag\text{-}fgr}$.

In an effort to understand the nature and possible structural relation between the v-*fgr onc* gene with other cellular genes of known sequence, we used the computer homology search programs of Wilbur and Lipman (*7*). This analysis revealed that v-*fgr* consists of portions of at least two distinct cellular genes, one of which is an actin, a cytoskeleton protein of 375 amino acid residues. Starting from amino acid position 141, we observed extensive homology between the v-*fgr* product and cytoplasmic actins derived from mammalian cells (*8*) (Fig. 2A). The sequence homology was greater than 98 percent with only two mismatches out of 128 amino acids. Four of these mismatched amino acids occurred at the amino terminal end of the actin gene, which appears to vary from one type of actin to the other. Beyond the 268th amino acid, the homology between these two proteins became statistically insignificant.

Immediately downstream of the actin-like sequence, the v-*fgr onc* gene product was found to be highly homologous to the *onc* moiety of P90$^{gag\text{-}yes}$, the primary translational product of the Y73 avian sarcoma virus (v-*yes*) (*9*). Thus, starting from amino acid position 269 and extending to 657, we observed an 80 percent amino acid sequence homology between these two polyproteins, with 311 out of 388 amino acids matching (Fig. 2B). The v-*fgr* encoded protein showed similar homology with the products of v-*src*, v-*abl*, v-*fes*, and v-*fps* (*5, 8, 9*). Thus, the v-*fgr* protein shared 288, 162, 156, and 155 amino acids with *src*-, *abl*-, *fes*-, and *fps*-coded transforming proteins, respectively (*5, 9, 10*). A reduced degree of homology was observed between v-*fgr* and v-*mos* coded gene products (*11, 12*), one of which was shown to be a protein kinase (*13*). A single site for tyrosine phosphorylation has been detected within p60^{src} (*14*). This residue has been located precisely at amino acid position 416 of the p60^{src} coded by the Prague strain of Rous sarcoma virus (*7*). The location of the phosphate acceptor tyrosine residue in p60^{src} is homologous to the tyrosine residue at amino acid position 553 of P70$^{gag\text{-}fgr}$ shown in Fig. 1. This tyrosine residue is preserved in all the tyrosine-specific kinases for which amino acid sequences are available (*5, 10*).

A stretch of 22 amino acids from position 118 to position 140 of P70$^{gag\text{-}fgr}$ exhibited no sequence homology with the FeLV *gag* gene, actin genes, or any retrovirus *onc* gene. The origin of these sequences is not clear. It is possible that this region represents the 5′ leader sequence of the actin gene which was incorporated during the recombination process that led to GR-FeSV. Since none of the actin genes from the cat has been sequenced, this possibility is not yet testable. Alternatively, this region may represent an upstream exon of c-*fgr*, in which case the recombination involving actin sequences occurred within c-*fgr*. The analysis of c-*fgr* (cat) locus will aid in the resolution of this question.

Within the v-*fgr*, the nucleotide sequence between 807 and 825 was found to contain sequence homology with both actin and v-*yes* genes (Fig. 3). It is possible that this sequence homology has allowed homologous recombination in this region. Such homologies also occur between helper virus and c-*onc* gene sequences in Moloney murine sarcoma virus, simian sarcoma virus, Abelson murine leukemia virus, and myelocytomatosis virus (*12, 15*). These findings have led to the speculation of homologous recombination between cell-derived proto-oncogenes and helper virus sequences during the generation of acute transforming viruses.

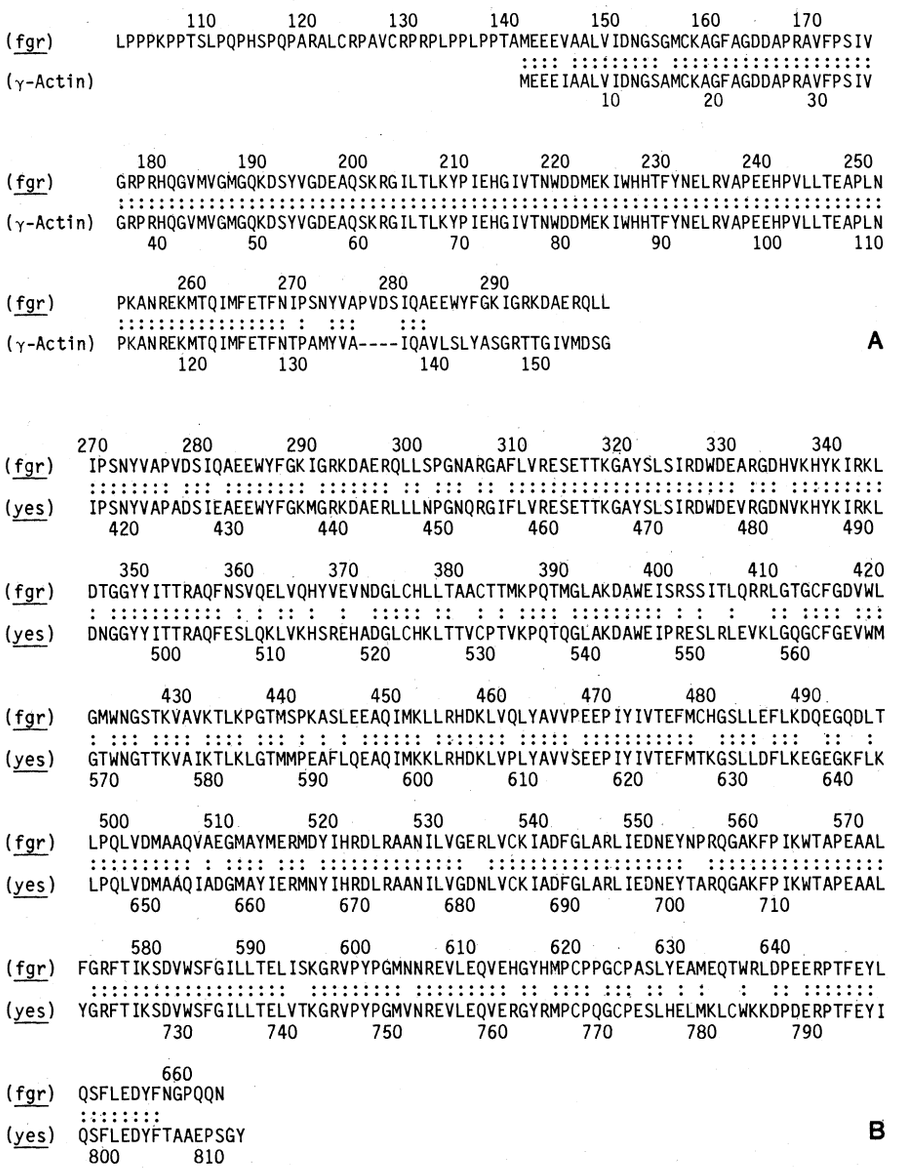

Fig. 2. Similarities between the deduced amino acid sequences of (A) v-*fgr* and actin gene products and (B) v-*fgr* and v-*yes* gene products. The amino acid sequences are aligned to give the maximal homology. For this purpose the computer methods described by Wilbur and Lipman (*7*) were used. A *K*-tuple size of 1, window size of 20, and gap penalty of 3 were used in this analysis. Dots indicated identical amino acids. A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; Y, Tyr.

Fig. 3. Sequence homology between v-*fgr*, actin, and v-*yes* genes. The v-*fgr* sequence corresponds to the nucleotide positions 808 to 825 presented in Fig. 1. The actin sequence is from (*8*) and v-*yes* sequence is from (*9*). Since the v-*yes* sequence shown in this figure is derived from chicken genome, there is considerable mismatching in the third base position of individual codons. The c-*fgr* (from the cat) sequences would be expected to show better homology in these positions.

```
Actin:    CCA GCC ATG TAC GTG GCC
          ||   | |  ||| ||| |||
v-fgr:    CCC AGC AAC TAC GTG GCC
          ||  ||| ||  ||  ||  ||
v-yes:    CCA AGC AAT TAT GTA GCT
```

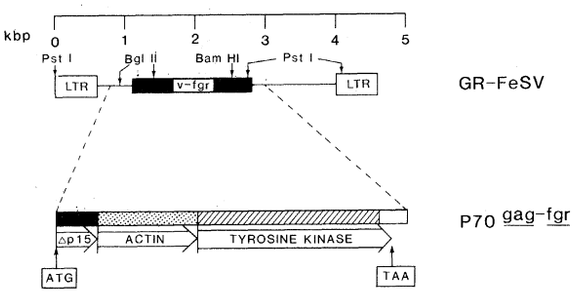

Fig. 4. Summary of the major structural features of the GR-FeSV genome. Important features of GR-FeSV genome including the open reading frame, important restriction enzyme cleavage sites, and the region of homology with FeLV p15, actin, and v-*yes* gene products are indicated. *LTR*, long terminal repeat; *kbp*, kilobase pairs.

Nucleotide sequence analysis of the proviral genome of GR-FeSV disclosed several important features concerning the genomic molecular organization (Fig. 4). Many of the acute transforming viruses appear to synthesize their transforming protein by means of a *gag-onc* hybrid molecule, the amino termini of which contain at least a portion of their respective *gag* structural proteins. In the case of GR-FeSV, the first 118 amino acids of the *gag-fgr* hybrid protein are derived from the FeLV p15 and the next 540 amino acids are coded by v-*fgr*. The last five amino acids of P70$^{gag\text{-}fgr}$ are coded by the FeLV envelope gene. However, the recombinational event occurred within the envelope gene, altering the reading frame and creating a terminator codon. Thus, the transforming protein utilized the helper viral sequences for the initiation and termination of its synthesis. This appears to be a common feature of many retroviral transforming genes and, in fact, may be essential for the activation of these genes (*9–12*).

A most interesting aspect of v-*fgr* relates to the finding that this oncogene contains two distinct domains, one derived from an actin gene and the other from a gene belonging to the tyrosine-specific kinase gene family, the latter being a constituent of a number of retrovirus-transforming genes. These findings imply that GR-FeSV arose as a result of interaction between helper virus DNA and two distinct cellular genes. Similar double recombinations seem to have occurred during the generation of Harvey and Kirsten murine sarcoma viruses (Ha-MuSV and Ki-MuSV), avian erythroblastosis virus (AEV), and avian MH_2 virus (*16*). In the case of Ha-MuSV, the viral genome arose by independent recombination of the Mo-MuLV with the rat c-Ha-*ras* gene and sequences from a replication defective, endogenous virus-like genome of rats (rat VL 30) (*16*). In the case of AEV, there is convincing evidence that this viral oncogene arose by recombination with two distinct loci of chicken cellular genome designated c-*erb-A* and c-*erb-B* (*16*). It therefore appears that some acute transforming retroviruses consist of two distinct cellular genes, suggesting their cooperative effect in the transformation process. In the case of GR-FeSV, we have been able to identify the biochemical nature of both genes involved in the genesis of its transforming gene.

The presence of actin sequences near the amino terminal region of P70$^{gag\text{-}fgr}$ raises interesting questions. Actin is a highly conserved and abundant structural protein and is present in all eukaryotic cells. Six actin isoforms are known in vertebrates: four muscle types and two nonmuscle types (*17*). Each muscle-type actin is functionally involved in muscle contraction and is expressed only in particular muscle tissues. Conversely, cytoplasmic actins participate in a variety of functions, such as cell motility, mitosis, and maintenance of the cytoskeleton, and are expressed in all cell types. Stable alterations of cell shape and motility have been considered as one of the phenotypic characteristics of transformed cells. In fact, human cells transformed by chemical carcinogens have been shown to express an aberrant form of β-actin (*18*). This aberrant form was found to contain a point mutation that was accompanied by subtle reduction in the incorporation of the of variant β-actin into the cytoskeleton of HuT 14 cells (*18*). There also appears to be some correlation between the appearance of the variant actins and increased ability of these cells to produce tumors in nude mice. It is therefore possible that the P70$^{gag\text{-}fgr}$ which contains 134 out of actin's 375 amino acids represents an aberrant form of this protein which interferes with the formation of proper cytoskeletal structure in cells transformed by GR-FeSV. Alternatively, the actin moiety of P70$^{gag\text{-}fgr}$ may serve to direct the tyrosine kinase to a limited set of targets in the cytoskeleton which would not normally be accessible for phosphorylation. The availability of molecular clones containing the GR-FeSV genome should make it possible to determine how the actin sequence of v-*fgr* relates to the biological activity of this virus.

GERMAN NAHARRO
KEITH C. ROBBINS
E. PREMKUMAR REDDY
Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, Maryland 20205

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