Proposal for Naming Host Cell-Derived Inserts in Retrovirus Genomes†

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We propose a system for naming inserted sequences in transforming retroviruses (i.e., *onc* genes), based on using trivial names derived from a prototype strain of virus.

A number of retroviruses have been isolated from naturally occurring or laboratory-induced tumors. Some of these are able to cause rapid disease in laboratory animals and to induce transformation of morphological and growth properties of appropriate tissue culture cells (for review, see 16, 19, 22). All such viruses whose genomes have been closely examined share a common feature: the presence of a nucleotide sequence which encodes a protein unnecessary for viral replication but required for the induction and maintenance of the transformed phenotype. When tested, such sequences have been found to be closely related to a sequence that occurs in the uninfected host cell yet is distinct from the genome of any endogenous viruses which might be present (2-15, 16a-18, 21, 23-54). The transformation-specific sequences have been generally referred to as onc genes (1a). There are at least 13 distinct onc genes which have been identified in about 20 isolates of transforming retroviruses (Table 1). It has been proposed that the transforming viruses have arisen by a mechanism involving recombination between virus and cellular information, with the consequence that an apparently normal cellular gene has come under the replicative and expression controls provided by the viral genome and, by virtue of modification in structure or mode of expression, has acquired the ability to cause cell transformation.

Although there is general agreement among workers in the field concerning the nature of *onc* genes and their relationship to the host cell, there is substantial confusion surrounding the names of these sequences and their cellular relatives. For example, the name *src*, originally used to designate the *onc* gene of Rous sarcoma virus, has recently been applied generally to sequences which are completely unrelated in sequence, nature of the gene product, and location in the genome. The use of identical names for genes of unrelated sequence and function can lead to serious problems in communication. An additional problem has arisen in the description of the endogenous cellular sequence related to an *onc* gene. The sequences related to the various *src* genes, for example, have been often called "sarc," with the result that the virus and the cellular sequences have identical pronunciations. More cumbersome designations for such sequences have been proposed, but not widely used.

It seemed necessary to establish a precise and generally accepted way of communicating about onc genes. For this purpose, the authors of this article have formed a committee which reports to the International Committee on Taxonomy of Viruses through the Retrovirus Study Group of that organization. The following is our proposal.

Retrovirus genes encoding replicative functions (i.e., gag, pol, and env) have been accorded three-letter names derived from their product or some other feature (1a). We propose that this system be extended to include the nonreplicative inserts found in many strains of retrovirus. By this proposed system, such inserts (or *onc* genes) will be given trivial three-letter designations. These names are not meant to imply specific diseases, target cells, or functions but rather are to be simply names of sequences which are not derived from viral replicative information and which encode a protein (or a portion of a polyprotein) likely to be involved in transformation of the infected cell. We also propose a system for distinguishing the viral from the related cellular sequences and, where necessary, the sequences in related viral strains from one another.

The names for these sequences are to be generated according to the following guidelines:

(i) The names should be three letters, lower-case italics.

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Name	Viral insert	Virus strain	Probable animal ori- gin	Protein product	References
rel	rel	Avian reticuloendotheliosis virus-T	Turkey		51
src	RSV-src B77-src rASV-src	Rous sarcoma virus B77 avian sarcoma virus Recovered avian sarcoma virus	Chicken Chicken Chicken, Japa- nese quail	pp60 ^{src} pp60 ^{src} pp60 ^{src}	10, 14, 26 10, 14 46, 48
	PR-RSV-src	Prague strain Rous sarcoma virus	Chicken	pp60 ^{src}	10, 14
myb	AMV-myb	Avian myeloblastosis virus strain BAI-A	Chicken		11, 13, 18, 41
	E26-myb	Avian leukemia virus strain E26	Chicken		13, 20
тус	MC29-myc	Avian myelocytomatosis virus MC29	Chicken	P110 ^{gag-myc}	6, 15, 25, 33, 35, 36
	CMII-myc	Avian myelocytomatosis virus CMII	Chicken	P90 ^{gag-myc}	
	MH2-myc	Avian myelocytomatosis and	Chicken	P100 ^{gag-myc}	15, 34
	OK10-myc	Avian myelocytomatosis virus OK10	Chicken	P200 ^{eag-pol-myc}	7, 31
erb-A erb-B	AEV-erb-A AEV-erb-B	Avian erythroblastosis virus Avian erythroblastosis virus	Chicken Chicken	P75 ^{gag.erb.A} p45 ^{erb.B}	5, 24, 28 30, 36, 53
fps"	FSV-fps PRCII-fps PRCIV-fps	Fujinami sarcoma virus PRCII sarcoma virus PRCIV sarcoma virus	Chicken Chicken Chicken	P140 ^{gag.fps} P105 ^{gag.fps} P170 ^{gag.fps}	23, 29 9 7a
yes	Y73-yes ESV-yes	Y73 avian sarcoma virus Esh sarcoma virus	Chicken Chicken	P90 ^{kag_yes} P80 ^{gag_yes}	27, 52 16a
ros	UR2-ros	UR2 avian sarcoma virus	Chicken	P68 ^{gag-ros}	1
mos"	Moloney- <i>mos</i> Gazdar- <i>mos</i>	Moloney murine sarcoma virus Gazdar murine sarcoma virus	Mouse Mouse		31a, 43a, 45 45
ras	Kirsten- <i>ras</i> Harvey- <i>ras</i> Rasheed- <i>ras</i>	Kirsten murine sarcoma virus Harvey murine sarcoma virus Rasheed rat sarcoma virus	Rat Rat Rat	p21 ^{ras} p21 ^{ras} P29 ^{gag.ras}	15a, 21, 40, 45 15a, 21, 40, 45 39
abl^a	abl	Abelson murine leukemia virus	Mouse	P120 ^{gag-abl b}	49, 50
fes	ST-fes	Snyder-Theilen feline sarcoma	Cat	P85 ^{rag.fes}	2, 37, 43
	GA-fes	Gardner-Arnstein feline sarcoma virus	Cat	P110 ^{µag.fes}	2, 43
fms"	MS-fms	McDonough feline sarcoma virus	Cat	P170 ^{gag.fms}	2
sis	sis	Simian sarcoma virus	Woolly mon- key		16a, 31b

 TABLE 1. Proposed names for onc genes

^a Some suggested pronunciations: *fps*, "fips"; *mos* as in "moss"; *abl* as in "able"; *fms*, "fems." ^b Size of the protein depends on viral strain.

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(ii) The names should be trivial; that is, no target cell specificity or functional significance should be implied, and they are to be considered as names of coding sequences only.

(iii) They are to be derived in some mnemonic way from the name of the prototype virus or viruses or from some other memorable feature of the viruses.

(iv) Related sequences in different viruses from the same species are to be called by the same name in a way that should point to the same cell sequence and the same or a closely related protein product, although it should not be necessary to have identified all of these to assign a name.

(v) When necessary for clarity, the differences between inserts in related viruses can be indicated by prefixing the name with the abbreviation or name for the virus or virus strain.

(vi) The related sequence found in the cell of origin will be designated with a lowercase "c-" preceding the sequence name, e.g., c-src. The animal species of the cellular homologue should be indicated in parentheses after the name of the sequence, e.g., c-src (chicken). The unadorned name will indicate the viral sequence only; however, where helpful for emphasis, it may be prefixed with "v-" (e.g., v-src).

(vii) Protein products will be designated according to current convention, using the approximate molecular weight $(\times 10^{-3})$ preceded by p (for protein), pp (for phosphoprotein), or P (for polyprotein), and followed by the name of the gene in superscript. Thus, pp 60^{src} , p 150^{c-abl} , and P $120^{sag-abl}$ stand for the product of src, the product of the endogenous cell sequences related to *abl*, and the polyprotein containing both gagant *abl*-specific information, respectively.

(viii) Should the same virus be found to have two independently expressed inserts (i.e., coding for different proteins through distinct mRNA's), then they can be distinguished by affixing -A, -B, etc., to the name (e.g., avian erythroblastosis virus *erb-A* and *erb-B*.)

(ix) Names along the same lines can also be given to nontransforming inserts if found in retroviruses or deliberately put there, but should be limited to genetically significant regions, i.e., those with a protein (or functional RNA) product. For example, htk could be used for the herpes simplex virus pyrimidine kinase gene inserted into a retrovirus vector (48a).

(x) In a case where somewhat different yet related inserts are found in viruses of different species, different names may be used (38).

(xi) Strict genetic evidence is not required to assign a name, but it should be shown (a) that the region is nonviral and (b) that it has either a protein or functional RNA product or a genetically identifiable function.

A list of suggested names is shown in Table 1. More names are likely to be added in the future. Several of the names on this list are already in use (e.g., src, myb, erb, fps). erb and myb were originally proposed with a different rationale, i.e., that they were indicative of transformed cell type (32). We do not consider transformed cell type to be a useful criterion for such assignments since many of the viruses cause a variety of diseases, at least seven of the onc sequences are in viruses that cause sarcoma as their most common disease, and even in those viruses that do cause a relatively unique definable disease (such as Abelson MuLV), there is no general agreement concerning the nature of the transformed cell. The names mentioned, however, should in this context be considered as trivial names derived from the name of the prototype virus. We suggest changing the name proposed for the transforming insert of avian myelocytomatosis virus MC29 and related viruses (mac; 32) to myc to match more closely the name of the prototype virus.

If the name of an onc gene is considered to describe a name of inserted sequence all or at least part of which induces a functional product. then (at least in principle) it can be precisely defined as that sequence which is unrelated to the genome of any replication-competent, nontransforming virus (i.e., not belonging to a gag, *pol*, or *env* gene or to some noncoding internal or terminal region of such a virus). With many of these sequences, it is quite difficult to obtain a definition by purely genetic techniques, since they are usually found in replication-defective viruses. In all cases, however, it is possible to use physical, biochemical, and recombinant DNA techniques to define the limits of *onc* sequences accurately, for example, by comparing nucleotide sequences of a transforming virus, its nontransforming but replication-competent helper, and the related cellular sequence or sequences with each other and with the amino acid sequence of the suspected gene product. A region of a genome defined in this way is not, in the strictest sense, a "gene." However, to refer to a defined sequence as an onc gene, although imprecise, should not create serious confusion so long as it is understood that not all of the sequence may be directly involved in encoding a product and that additional viral sequences may encode part of the final gene product.

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