quence homology occurs between amino acid residues 89 and 120 of FP when compared with CRP and SAP. Both amino- and carboxyl-terminus regions of FP have greater similarity to SAP than to CRP.

To examine whether the dual regulation of FP synthesis results from an effect of sex steroids and mediators of acute inflammation on a single gene or from their independent actions on two or more genes or gene copies, we analyzed restriction fragments of high molecular weight DNA by Southern blotting using FP-specific cDNA (*10*). Female hamster genomic DNA digests with ten restriction enzymes all resulted in single bands when Southern blots were probed with nick-translated pFP1 (Fig. 2) (*11*). In seven digests, restriction fragments containing FP-specific DNA were less than 4.26 kilobases (kb) in length. These data suggest that FP is encoded by a single gene locus.

The FP-specific cDNA insert was then used to examine basal concentrations of FP hepatic messenger RNA (mRNA) in normal female and male hamsters as well as in males 48 hours after induction of a sterile abscess with an intramuscular injection of turpentine (Fig. 3). FP-specific mRNA is 1 kb in length and is present in large quantities in female hamster liver in the resting state. FP mRNA was detected in small quantities in livers of unstimulated male hamsters and in increased quantities in the liver of stimulated male hamsters. Relative contents of FP mRNA corresponded to the relative concentrations of FP in serum of the animals from which liver mRNA was isolated (*12, 13*). In addition to the major species of FP-specific mRNA, at least two discrete species of higher molecular weight were noted in female and male hamster livers (Fig. 3). These may represent cross-reactivity of the FP probe with an mRNA species encoding other inducible sex-limited proteins or, more likely, precursor forms of the major FP-specific mRNA.

Messenger RNA from the liver of normal females and males 48 hours after tissue injury directed the synthesis of an FP primary translation product of 27.5 kilodaltons (kD) (Fig. 3) (*14*). Little or no FP was synthesized under cell-free translation conditions by mRNA isolated from plasma of a resting male hamster.

These findings support the utility of FP as a model for examining the regulation of protein synthesis by mediators of acute inflammation and by sex steroids. The evidence suggests that pretranslational regulation of FP synthesis is a function of these two factors.

Female protein shares greater amino acid sequence homology with human SAP than with CRP, even though the property of Ca^{2+}-dependent binding to phosphorylcholine is characteristic of both CRP and FP whereas the Ca^{2+}-dependent binding to agarose is shared by FP and SAP (*1*). Isolation of genomic clones for FP should help elucidate the structure of the FP gene and provide insight into control elements that take part in the regulation of FP biosynthesis by sex steroids and mediators of acute inflammation.

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A New Class of Endogenous Human Retroviral Genomes

Abstract. *Human DNA contains multiple copies of a novel class of endogenous retroviral genomes. Analysis of a human recombinant DNA clone (HLM-2) containing one such proviral genome revealed that it is a mosaic of retroviral-related sequences with the organization and length of known endogenous retroviral genomes. The HLM-2 long terminal repeat hybridized with the long terminal repeat of the squirrel monkey virus, a type D retrovirus. The HLM-2* gag *and* pol *genes share extensive nucleotide sequence homology with those of the M432 retrovirus (a type A–related retrovirus), mouse mammary tumor virus (a type B retrovirus), and the avian Rous sarcoma virus (a type C retrovirus). Nucleotide sequence analysis revealed regions in the HLM-2* pol *gene that were as much as 70 percent identical to the mouse mammary tumor virus* pol *gene. A portion of the putative HLM-2* env *gene hybridized with the corresponding region of the M432 viral genome.*

Some members of Retroviridae (*1*) can induce tumors in many species of mammals. Retroviruses classified by morphologic criteria as type A, B, C, and D viruses (*2*) are associated with various types of malignancy. Although many of these retroviruses induce tumors as infectious agents, they can also be transmitted as endogenous proviral genomes through the germline. Recent studies have revealed endogenous retroviral sequences in multiple copies within the genomes of animals and humans. One class of human endogenous retroviral sequences has been shown to be related to known mammalian type C viruses (*3*). A distinct class of human endogenous retroviral sequences has been detected and molecularly cloned with the mouse mammary tumor viral (MMTV) genome (prototype B virus) as a probe (*4*).

Evidence has accumulated showing that there have been genetic interactions between different retroviral classes during their evolution. Such interactions have been implied by immunologic cross-reactivities detected among respective structural proteins of these agents as well as by molecular hybridization (*5*). We now describe a human recombinant clone (HLM-2) that con-

tains sequences related to MMTV *gag* and *pol* genes (*4*) and its relation to prototype viruses representing each of the major retroviral classes.

Three purified restriction fragments from HLM-2 recombinant DNA (designated 1, 2, and 3; Fig. 1A) were digested with various restriction enzymes and then analyzed by Southern blot hybridization at low stringency to define regions containing retroviral-related sequences (*4*, *6*). Southern transfers of DNA from fragment 1 digested with Hind III (4.0 to 8.0 HLM-2 map units; Fig. 1A) were hybridized to ^{32}P-labeled recombinant M432 DNA [related to type A retroviruses (*7*)], MMTV (*8*), and the type D squirrel monkey retrovirus (SMRV) proviral DNA (*9*). A 1.5-kilobase (kb) fragment that reacted with each of the probes (Fig. 1, A and B) was identified. In addition, SMRV hybridized weakly to a 0.9-kb Hind III fragment. Additional restriction enzyme analysis showed that this region of homology extends from 4.0 to 4.9 HLM-2 map units.

Fragment 2 (8.0 to 11.6 HLM-2 map units; Fig. 1A) was digested with Eco RV plus Xho I, yielding four smaller fragments. Again, each of the viral probes gave a strong signal with 1.5- and 0.8-kb Eco RV fragments (Fig. 1C). The boundaries of this region of homology were defined further by analysis of Pst I–digested fragment 2 (Fig. 1C). Because each probe reacted with the 0.4- and 1.6-kb fragments, we conclude that the boundaries of this region of contiguous homology are defined by the Hind III site at 6.5 map units in fragment 1 and by the Pst I site at 10 map units in fragment 2 (Fig. 1A).

Fragment 3 (11.6 to 13.2 HLM-2 map units) contains single restriction sites for Sst I, Pst I, and Pvu II (Fig. 1A). Although the MMTV probe did not hybridize to fragment 3 DNA, the SMRV probe reacted with Pst I and Pvu II fragments as well as with the 0.9-kb Sst I fragment (Fig. 1D). Because sequences within the 0.9-kb Sst I–Eco RI fragment are repeated at 4.0 to 4.9 HLM-2 map units, they appear to define long terminal repeat (LTR)–like elements. The M432 probe also reacted with fragment 3 DNA (Fig. 1D). These viral-related sequences are immediately adjacent to the SMRV-related LTR-like structure (Fig. 1A). The M432 and *Mus musculus* intracisternal type A particle genomes also share a region of major internal homology and a 0.6-kb region of homology adjacent to their 3′ LTR-like elements (*7*).

Reciprocal hybridization experiments with the three HLM-2 fragments as probes confirmed these results and showed that the retroviral-related sequences in HLM-2 DNA are organized in a manner consistent with that of a genetically transmitted proviral genome. The major region of homology between the viral genomes and HLM-2 DNA spans the 3′ half of the *gag* gene through the entire *pol* gene (6.5 to 10.0 HLM-2 map units). It seems likely that the region between 10.0 and 12.3 HLM-2 map units represents the *env* gene of this proviral genome. Consistent with this possibility is the homology between the M432 viral *env* sequences and HLM-2 DNA within the region 11.6 to 12.3 map units (Fig. 1A).

To confirm the orientation of the viral-related sequences in HLM-2 and to identify more precisely the conserved regions of the *pol*-related sequences, we determined the nucleotide sequence of the 3.6-kb Eco RI fragment (8.0 to 11.6 HLM-2 map units; Fig. 1A). A comparison of a portion of this nucleotide sequence (nucleotides 1451 to 1975) and the translated amino acid sequence with those of *pol* genes from other infectious retroviruses (Fig. 2 and Table 1) revealed four regions of homology between HLM-2 and MMTV, SMRV, RSV (avian Rous sarcoma virus), and HTLV-I (human T-cell leukemia virus). No comparable sequence homology was observed between HLM-2 and the *pol* gene of Moloney murine leukemia virus (*10*).

The β subunit of the RSV reverse transcriptase is cleaved into the α subunit and a 32,000-dalton peptide (pp32) (*11*). The pp32 peptide contains an endonuclease activity specific for closed circular proviral DNA (*12*). A comparison of the HLM-2 and RSV amino acid sequences revealed a region of appreciable homology between nucleotides 1595 to 1712 (Fig. 2). This portion of the RSV *pol* gene corresponds to the amino terminus of the pp32 peptide (*13*). The junction between the analogous HLM-2 α subunit and pp32 peptides must occur at or near nucleotide 1594. Again with the RSV sequence as a reference, this alignment

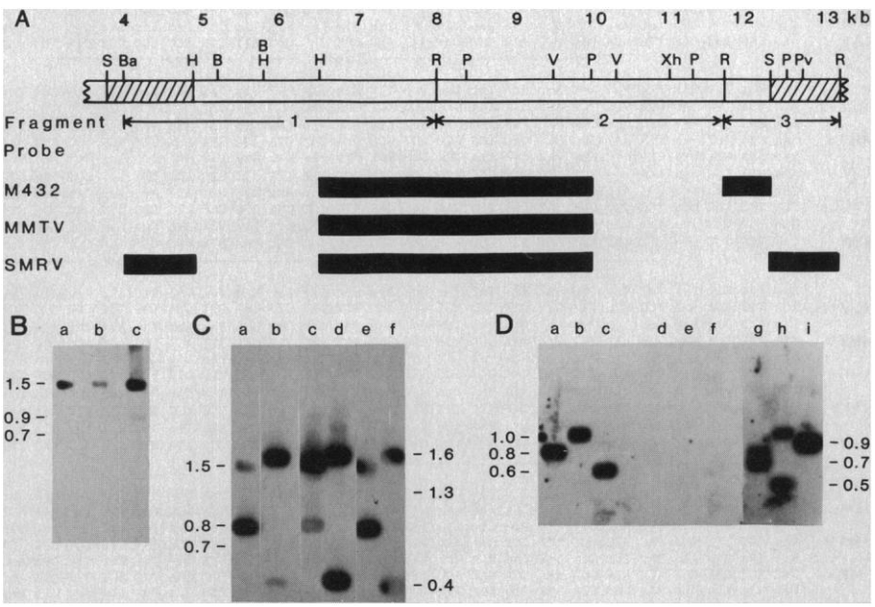

Fig. 1. Identification of retroviral-related sequences in HLM-2 recombinant DNA. Three HLM-2 restriction fragments were purified by agarose gel electrophoresis and digested with the indicated enzymes. The restricted DNA's were then subjected to electrophoresis through 0.8 percent agarose gels and transferred to nitrocellulose filters by the method of Southern (*9*). Hybridizations were carried out as described (*4*) with 2×10^6 count/min of the indicated proviral DNA probes per milliliter. The probes were labeled with ^{32}P by nick translation (*17*) to a specific activity of 2×10^8 count/min per microgram. Filters were washed in 3× standard saline citrate and 0.1 percent sodium dodecyl sulfate at 55°C and subjected to autoradiography for 2 to 5 days. (A) A diagrammatic summary of the hybridization data. The relevant restriction sites are designated on a partial map of the HLM-2 recombinant DNA (*4*). Regions of homology between HLM-2 and the proviral genomes are represented by solid bars, and sequences repeated within the recombinant clone are indicated by the cross-hatched region of the HLM-2 map. Abbreviations: S, Sst I; Ba, Bam HI; H, Hind III; B, Bgl II; R, Eco RI; P, Pst I; V, Eco RV; Xh, Xho I; and Pv, Pvu II. (B) HLM-2 restriction fragment 1 digested with Hind III and probed with M432 (lane a), MMTV (lane b), and SMRV (lane c). (C) HLM-2 restriction fragment 2 digested with Eco RV plus Xho I (lanes a, c, and e) and Pst I (lanes b, d, and f) and probed with M432 (lanes a and b), MMTV (lanes c and d), and SMRV (lanes e and f). (D) HLM-2 restriction fragment 3 digested with Pst I (lanes a, d, and g), Pvu II (lanes b, e, and h), and Sst I (lanes c, f, and i) and probed with M432 (lanes a to c), MMTV (lanes d to f), and SMRV (lanes g to i). The sizes of the restriction fragments are in kilobases.

also suggests that the termination signal for the HLM-2 *pol* gene should occur near nucleotide 2428. Consistent with this prediction is the presence of a termination codon in the reading frame (see Fig. 2) beginning at nucleotide 2421 of the HLM-2 sequence.

The HLM-2 proviral genome is representative of a family of human endogenous viral sequences, comprising as many as 50 copies (*14*). Our results distinguish this family from human endogenous viral sequences related to mammalian type C viruses (*3*). The HLM-2 genome showed no detectable homology

Table 1. HLM-2 nucleotide and amino acid sequence homology with other retroviral *pol* genes (see Fig. 2). Spaces inserted into the sequence to maximize the homology were included in the calculation of percentage homology.

Retroviral *pol* gene	Homology (percent)									
	Nucleotides 1451 to 1975		Nucleotides 1469 to 1517 (Region 1)		Nucleotides 1595 to 1712 (Region 2)		Nucleotides 1811 to 1850 (Region 3)		Nucleotides 1892 to 1975 (Region 4)	
	Base pairs	Amino acids	Base pairs	Amino pairs	Base pairs	Amino acids	Base pairs	Amino acids	Base pairs	Amino acids
MMTV	51	45	54	63	69	67	55	59	64	71
SMRV	50	38	52	50	70	72	61	53	58	57
HTLV	37	27	48	50	44	38	45	47	52	46
RSV	44	33	50	38	55	54	53	47	54	64

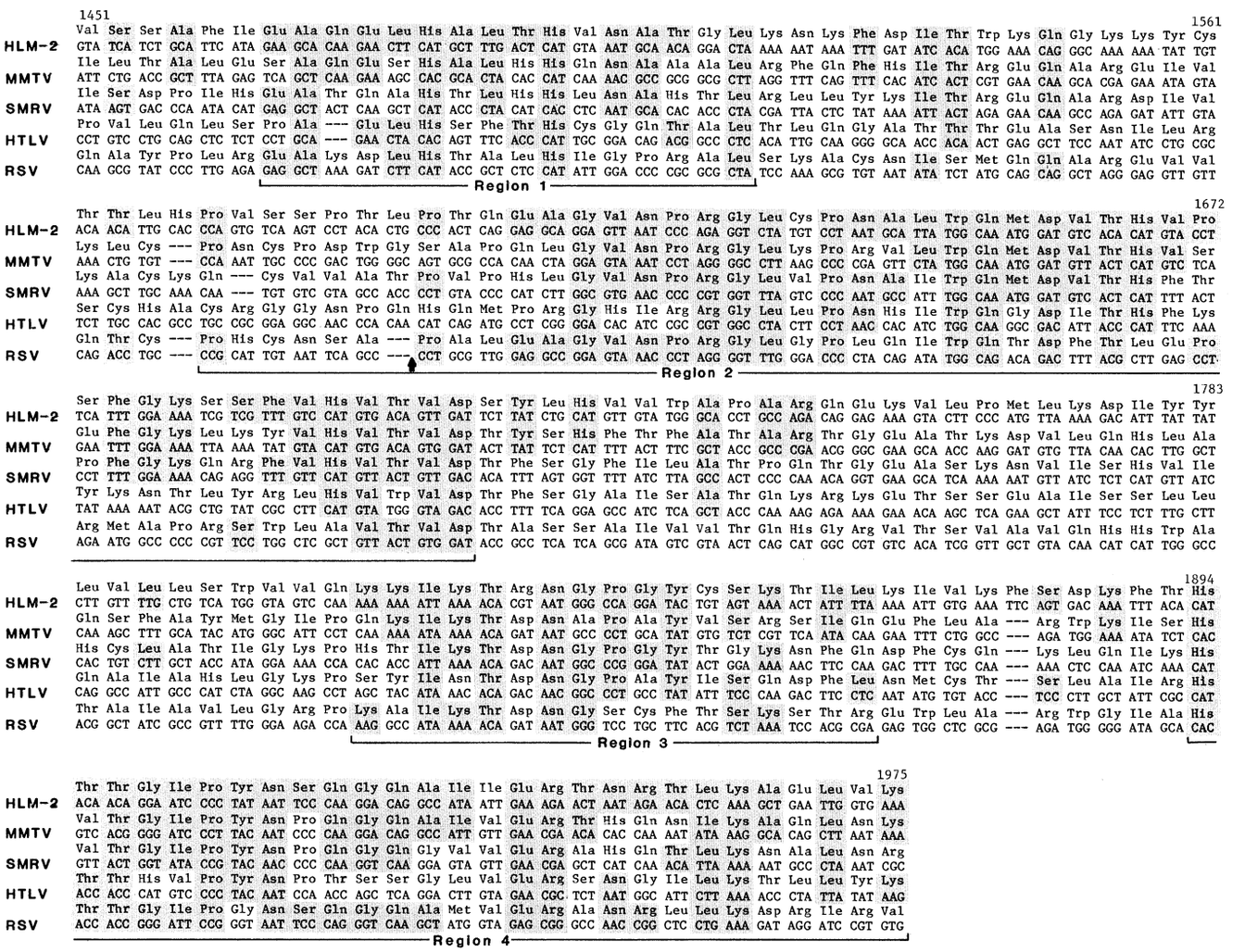

Fig. 2. Alignment of amino acid and nucleotide sequences of HLM-2 and infectious retroviral *pol* genes. The nucleotide sequence of the HLM-2 3.6-kb Eco RI fragment (8.0 to 11.6 map units; see Fig. 1A) was determined by the dideoxynucleotide chain termination method on M13 subclones containing portions of the Eco RI fragment (*18*). The optimum deduced amino acid sequence homology between HLM-2 and MMTV (*19*), RSV (*20*), HTLV-I (*21*), and SMRV (*5*) was determined by means of the PRTALN computer program (*22*). Gaps were introduced in the sequences to maximize the extent of homology between HLM-2 and the other retroviral *pol* genes. The MMTV sequence determined by us differs from that determined by Redmond and Dickson (*19*) by the insertion of CC at nucleotides 181 and 182 and G at nucleotide 280 (*5*). The arrow indicates the potential junction between the RSV *pol* α subunit and pp32 peptide (*13*). Abbreviations for bases: G, guanine; C, cytosine; T, thymine; A, adenine. Amino acid residues are abbreviated by the standard three-letter notations.

with mammalian type C viruses by low-stringency blot hybridization or comparative nucleotide sequence analysis. In contrast, the HLM-2 *pol* gene showed appreciable homology not only with type B retroviruses but with type A, avian type C, and type D retroviruses as well. These findings are consistent with the known functional similarities in the requirement for divalent cations for each of these viral polymerases as well as with other studies indicating genetic relations between their *pol* genes (*5*).

The HLM-2 genome represents a mosaic of sequences characteristic of different retrovirus classes. It has *env* gene sequences most closely related to the type A virus, LTR sequences most homologous with the type D virus, and *pol* gene sequences related to each of these as well as to mammalian type B and avian type C viral genomes. Although HLM-2 also showed distant homology with HTLV-I in its *pol* region, HTLV-I is not endogenous to human cells (*15*) but is transmitted horizontally as an infectious, tumor-inducing virus of humans (*16*). Whether the HLM-2 human retroviral-related sequences are expressed or are etiologic agents of human neoplasia is unresolved.

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Naturally Occurring Antibodies Reactive with Sperm Proteins: Apparent Deficiency in AIDS Sera

Abstract. *A set of naturally occurring immunoglobulin M (IgM) antibodies that are reactive with a defined subset of proteins in the acrosomal cap region of human sperm has been identified. These antibodies are present in a broad spectrum of human sera from males and females, 1 day to 40 years of age, and are absent or markedly deficient in a large proportion of sera from individuals with the acquired immune deficiency syndrome (AIDS) or at risk for AIDS. The subset of proteins with which the IgM antibodies are reactive includes a factor (or factors) capable of inhibiting lectin-induced T-lymphocyte proliferation. The prevalence of the sperm-reactive IgM antibodies indicates that they are not elicited by sperm. Further, immunoreactivity of the sperm proteins resulting in depletion of specific circulating IgM antibodies, or other interactions between the sperm proteins and elements of the immune system, may be a factor in the suppressed state of the immune system in AIDS.*

In the course of our studies on the proteins of mammalian spermatozoa (*1*), we have identified a set of immunoglobulin M (IgM) antibodies in human serum that, although immunologically reactive with defined components of human sperm, appear to be normal constituents of circulating Ig's. This inference is based on the finding that these antibodies are present in more than 99 percent of

Table 1. Presence or absence of IgM antibody reactive with acrosomal cap region of human sperm in sera from individuals with and without (control) AIDS or ARC.

Group	Status or type of donor	Sera examined (number)	Sera positive for IgM antibody* (number)	Sera negative for IgM antibody*	
				Number	Percent
	Homosexual males				
AIDS or at risk for AIDS	No symptoms	14	11	3	21
	ARC	45	30	15	33
	AIDS	20	12	8	40
	Others†				
	No symptoms	9	8	1‡	
	ARC	3	3	0	
	AIDS	1	0	1‡	
	Total	92	64	28	
Control	Adult males§	45	44	1	
	Adult females§	35	35	0	
	Hospitalized adults‖	21	21	0	
	Hospitalized children¶	30	30	0	
	Total control	131	130	1	

*IgM antibodies reactive with acrosomal cap region of human sperm (see Fig. 1). †Intravenous drug users, hemophiliacs, and infants born to women with AIDS. ‡Female prostitute. §Sera obtained from routine medical examination (sexual preference not known.) ‖From miscellaneous hospital admissions (for diseases other than of the immune system). ¶Ages, 1 day to 2 years; hospitalized for other than immune system diseases.