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# In vitro properties and experimental pathogenic effect of three strains of feline immunodeficiency viruses (FIV) isolated from cats with terminal disease

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## ABSTRACT

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Three strains of virus isolated from peripheral blood mononuclear cells (PBMC) of sick cats were identified as feline immunodeficiency virus (FIV) on the basis of in vitro cytopathic effect, T-lymphotropism, ultrastructural morphology and magnesium-dependent reverse-transcriptase activity. The pathogenic properties of two isolates were studied in 13 experimentally infected cats. The primary phase of infection was characterised by a range of haematological (neutropenia, lymphopenia, presence of atypical lymphocytes) and clinical alterations (fever, various signs lasting several weeks, generalised lymphadenopathy persisting for several months) and specific seroconversion. A correlation between the inoculated dose of virus and the intensity and duration of clinical signs was observed. The primary phase was followed in the 10 surviving cats by a stage of asymptomatic seropositivity of undetermined duration but which has persisted for over 35 months for the earliest infections. Viruses reisolated several weeks or months after experimental infection retained the same in vitro properties as the initial isolates.

## INTRODUCTION

Two pathogenic representatives of the Oncovirinae subfamily are known in the cat: feline leukemia virus (FeLV, Jarret et al., 1964; Rickard et al., 1969) causes a chronic immunodeficiency syndrome and the development of lymphoid or myeloid malignancies and feline sarcoma virus (FeSV), a natural recombinant of FeLV, can induce rapidly progressing fibrosarcomas (Snyder and Theilen, 1969; Irgens et al., 1972; Hardy, 1981).

In early 1987 the isolation of a lentivirus from cats with various diseases (Pedersen et al., 1987) aroused much interest within the scientific community; this virus, initially designated feline T-lymphotropic virus (FTLV) is now known as feline immunodeficiency virus (FIV). Frequent clinical observations of immunodeficiency-like syndromes in FeLV-negative cats led us to attempt viral isolation under the optimal conditions defined by Lévy (1985) for the human immunodeficiency virus (HIV). In the present work, we describe the biological properties of 3 isolates identified as FIV.

## MATERIALS AND METHODS

### *Isolation procedure*

A similar procedure to that described by Pedersen (1987) was used. Heparinised blood obtained by jugular venipuncture was separated on a Ficoll-sodium diatrizoate gradient (Histopaque-1077, Sigma, St Louis, MO, USA). The peripheral blood mononuclear cells (PBMC) layer was removed, washed 3 times in PBS buffer and resuspended to a concentration of  $10^6$  cells/ml in RPMI-1640 medium containing HEPES buffer, 10% foetal bovine serum, 5  $\mu\text{g}/\text{ml}$  concanavalin A (Con A), 100 U/ml penicillin and 100  $\mu\text{g}/\text{ml}$  dihydrostreptomycin. Three days after Con A-stimulation, the non-adherent lymphocyte-rich cell fraction was removed, centrifuged and resuspended in fresh culture medium to the same concentration. Cocultures were prepared by mixing equal volumes of 3-day Con A-stimulated PBMC cultures, one of which was prepared from a cat suspected to be infected by FIV and the other from a normal cat; recombinant human interleukin-2 (IL2) (Genzyme, Boston, MA, USA) was added to in the medium (100 U/ml). Pedersen et al. (1987) and Harbour et al. (1988) reported that 7-d old cultures obtained under these conditions contained 95–97% T-lymphocytes. On day 7, the flasks were enriched with 3-d Con A-stimulated PBMC from a healthy cat as follows: the content of flask (8 ml) was centrifuged and the pellet resuspended in 2 ml of complete medium. Simultaneously a fresh 3-d Con A-stimulated culture (8 ml adjusted to  $0.5 \times 10^6$  cells/ml) was resuspended in the same manner; the two fractions were then mixed together and the volume brought to 8 ml. This operation was repeated four times at intervals of 7 d.

### *Reverse-transcriptase activity*

Magnesium-dependent reverse-transcriptase (RT) activity was assayed in coculture supernatants according to the method optimised by Rey et al. (1984). Supernatants were ultracentrifuged for 5 min at 95 000 rpm (Beckman UC TL 100) and RT activity was measured in pellets maintained in 0.1% NTE-Triton buffer with a beta counter.

### *Animals*

Three domestic short-haired adults cats living with their owners in different suburbs of Paris were the source of virus; these cats (Nos 1, 2 and 3) were negative for FeLV and feline coronavirus and presented signs suggestive of an immunosuppressive condition (Table 1). Cat 1 had leucopenia (1200 leucocytes per ml) and severe lymphopenia (24 lymphocytes per ml) but blood tests were not performed on the other two cats. The severity of the clinical state of the diseased cats prompted their owners to request euthanasia in the days following virus isolation.

Experimental cats used both for in vitro (PBMC preparation) and in vivo studies (experimental infection) were obtained either from our own breeding colony or from a commercial breeder (IFFA-Credo, St. Germain sur l'Arbresle, Rhône, France). The animals raised in our cattery had been regularly tested for FeLV and coronavirus infections and were housed under strictly controlled sanitary conditions but without air or food sterilization. Those obtained commercially were originally specific pathogen-free (SPF) kittens; they were introduced into the experimental cattery and housed under usual conditions.

### *Experimental design*

Thirteen kittens, 3 to 7 months old, were inoculated with positive cultures or blood samples from experimentally infected cats (Table 2). The studies were conducted with the strains Wo and Me isolated from cats 1 and 2 and considered as potentially highly pathogenic on the basis of their in vitro properties. The RT activity of some doses was determined and found to range

TABLE 1

Clinical conditions of cats from which FIV were isolated

Ref. of cases	Sex	Age (years)	Clinical history	Ref. of isolates (date)	Outcome
No. 1	Neutered male	12	Anorexia and fever for 15 d, aregenerative anemia, severe lymphopenia	Wo (June 88)	Euthanized within a few days of virus isolation.
No. 2	Neutered male	10	Anorexia and fever, lethargy, severe depression	Me (Dec 88)	Idem
No. 3	Male	8	Diverse recurrent symptoms, lethargy, deterioration of general condition, gingivitis submaxillary adenitis, oral ulcerations	Le (Jan 89)	Idem

TABLE 2

Protocol of experimental inoculations: the route is IP except for Fa IV inoculated

Ref. of assay	Inoculates				Experimental cats	
	Isolate form	Volume (ml)	RT <sup>2</sup> activity	Date of inoculation	Name	Age (in months)
a	Me U.C. <sup>1</sup> supernatant coculture (initial isolation, day 14)	1.5	210	0.1.24.89	Gu	6
		0.5	70		Ma	6
		0.2	30		Pi	6
b	Me Supernatant coculture (Reisolation, day 13)	3	3	04.05.89	Pl	7
		3	3		Do	7
c	Wo Supernatant coculture (Initial isolation, day 13)	1		09.16.88	Ne	3
		0.5			So	3
		0.5			Tr	3
d	Wo Whole coculture (Initial isolation, day 24)	1		0.7.18.88	Et	3
		0.5			Vr	3
e	Me Blood from Gu 17 days p.i.	5		02.10.89	Pa	5.5
	Me Blood from Pa 24 days p.i.	5		03.06.89	Bi	6
	Wo Blood from Ne 7 weeks p.i.	5		11.04.88	Fa	3

<sup>1</sup>Ultracentrifugated 30 min. at 100 000g<sup>2</sup>Reverse transcriptase activity (cpm × 10<sup>-3</sup>)

from 3 to 210 (cpm × 10<sup>-3</sup>). Post inoculation (p.i.) the animals were monitored for clinical signs of disease. Samples were collected for haematological, virological and serological studies at various intervals as described in Tables 4 to 6 and Fig. 1.

#### *Histological examination*

Popliteal lymph nodes were resected at 10 weeks, 12 weeks and 11 months p.i. from three cats and mesenteric and ileocecal lymph nodes were obtained at autopsy from Cat Ne. Samples were fixed in Bouin's solution and embedded in paraffin wax. Sections 4 µm thick were stained with hemalun-eosin-saffron and the Giemsa slow method.

#### *Electron microscopy (EM)*

Samples were fixed in 2.5% glutaraldehyde and then in 1% osmic acid. Cacodylate buffer (0.2 M, pH 7.2) was used as diluent for fixation and as intermediate washing medium. After fixation, cells were dehydrated in an ethanol gradient and embedded in 100 glycidäther resin (Merck). Sections were cut with a Reichert ultramicrotome, stained with uranyl acetate and lead citrate, and examined with a JEM 100 CXII transmission electron microscope.

#### *Serological investigations*

Antibodies to FIV were detected by indirect immunofluorescence assay (IFA) and ELISA. For IFA we used 10-d cocultures prepared from Cats Vr

and Tr as antigen; using a procedure similar to that described by Yamamoto et al. (1988). Briefly, the infected cells were distributed into Teflon-wells on glass slides ( $7 \mu\text{l}$  per well), fixed in acetone (10 min at  $-20^{\circ}\text{C}$ ) and then treated with serum samples. With post-infected sera, 100% of the cells were fluorescent; the antibody titre was taken as the inverse of the dilution which reduced this fluorescence by 50%.

Serum samples were tested for antibodies to feline syncytium-forming virus (FeSFV) by IFA using a viral strain and a monoclonal antibody obtained by Chappuis (1974). The infected Crandell Feline Kidney (CrFK) cell line fixed at the onset of cytopathic effect (CPE) was used as antigen.

Antibodies to FIV were detected by a commercial kit (Petchek, Idexx, Portland, ME, USA) with the American petaluma strain as antigen.

FeLV-P27 antigen was detected using a commercial kit (Leukassay II, Pitman-Moore, NJ, USA).

### *In vitro virus infectivity*

*Assays in primary lymphoid cells.* The pellet of 3-d Con A-stimulated culture was pretreated with polybrene ( $2 \mu\text{g}/\text{ml}$ ) for 1 h at  $37^{\circ}\text{C}$  and incubated with supernatant of an infected coculture (1 h at  $37^{\circ}\text{C}$ ). The cells were then resuspended in complete medium in the presence of IL2. Fresh cells were added every 7 d to maintain cell concentration of the culture at about  $10^6$  living cells/ml.

*Assays in different cells lines.* Attempts were made to grow isolates in CrFK, SK, feline embryonic lung (FEL) and feline embryo (FE); confluent cells of untreated and polybrene or DEAE-dextran pretreated cell lines were inoculated with supernatant of infected cultures. Three sequential passages were performed using either supernatant or medium plus cells dispersed by trypsinisation as inoculant.

## RESULTS

### *Characterisation of the isolates*

Cell aggregation, syncytium formation, ballooning degeneration and cell lysis were observed within 1–4 d of cultivation (Table 3). A progressive alteration of the cultures beginning on day 21 was noted and cultures had to be discarded shortly after. The cultures were tested for FeLV-p27 antigen by ELISA and for FeSFV by IFA with negative results. Magnesium-dependent RT activity was detected in the three coculture fluids at day 7, the first day of assay; values peaked on day 14, then began to drop around day 21. In contrast, manganese-dependant RT activity was very low or negative.

Viral particles with characteristic lentivirus morphology were identified by

TABLE 3

Time of appearance of CPE in vitro for the three FIV isolated from sick cats

Method of virus propagation	Source of virus (Name)	Time for CPE (in days)	Mg <sup>2+</sup> (Mn <sup>2+</sup> ) dependant RT-activity <sup>1</sup>			
			7	14	21	
Coculture from spontaneously infected cats	PBMC <sup>2</sup> from cat:	No. 1 (Wo)	2			
		No. 2 (Me)	3	20	140	
		No. 3 (Le)	4		128	10
Coculture from experimental cats	PBMC from cat:	Gu, 2 m p.i.	1	120	190 (0.05)	1400
		Gu, 4 m p.i.	4	400	360 (0.8)	110
		Tr, 5 m p.i.	2			
		Tr, 21 m p.i.	3			
		So, 9 m p.i.	4	5	35 (0.5)	890
		Vr, 3 m p.i.	3	40	280 (5)	210
		Vr, 9 m p.i.	4	5	35	890
		Fa, 24 m p.i.	2			
Primary lymphoid cells.	Sup. coc. <sup>3</sup> from cat:	No. 1 (Wo)	3			
		No. 2 (Me)	1	21	210	
		Vr (Wo)	1	120	640	210

<sup>1</sup>cpm × 10<sup>-3</sup><sup>2</sup>Peripheral blood mononuclear cells<sup>3</sup>Supernatant coculture

EM examination of cultures but no virions of spumaviral or oncoviral morphology were observed.

### *In vitro infectivity*

Growth of the isolates in primary activated lymphoid cells was confirmed by the development of RT activity and of CPE identical to that observed in the initial cocultures. All attempts to replicate the viruses in feline cell lines yielded negative results.

In conclusion, the nature of CPE, the tropism for T-lymphoid cells, the magnesium-dependence of the RT activity and the morphology in EM allow us to identify the three isolates as feline lentiviruses.

### *In vivo infectivity*

Successful experimental transmission was demonstrated by seroconversion in all the inoculated animals and the re-isolation of viruses exhibiting the same properties from their blood. The fact that infection was transmitted by inoculation of cell-free supernatants confirms that FIV contamination does not necessarily take place via infected cells but can also be transmitted via cell-free virions as is the case for HIV.

The experimental cats developed a range of general signs (anorexia, depression, fever, weight loss) 3–6 weeks p.i. These clinical disorders peaked around the seventh week and were associated in some cats with localized infections (conjunctivitis, rhinitis, diarrhoea, gingivitis and infestation with ear mites). In three cats the clinical course was particularly severe: cat Et died abruptly 7 weeks p.i. following 48 h of depression and pronounced pallor of the mucous membranes and, although the cause of death was not determined in this animal, specific seroconversion was established; cat Ne started to present general signs associated with rhinitis and conjunctivitis from day 38 p.i., and, at the seventh week, extreme depression and agranulocytosis (Fig. 1) prompted a decision to euthanase the animal. Post-mortem examination revealed severe hypertrophy of ileocecal lymph nodes and a slight congestion of the small intestine. Histological examination of this organ revealed no lesions consistent with infectious panleukopenia and the absence of parvovirus in the faeces ruled out this possibility; cat Gu developed a variety of clinical signs 3 weeks after inoculation which remained severe for 2 months (Tables 4 and 5; Fig. 1) and then progressively decreased and completely disappeared; however, neutropenia persisted 17 months and the cat died 18 months p.i. after 48 h of depression, dehydration and anorexia. The other cats re-

TABLE 4

Intensity of clinical signs after experimental inoculation

Cats	Inoculate		Clinical score		
	Ref. <sup>1</sup>	RT <sup>2</sup>	Fever	Others clinical signs	Conclusions
Gu	a	210	+++	Anorexia, lethargy, weight loss, recurrent cutaneo-mucuous inflammation, ear mites	+++
Ma	a	70	+	0	+
Pi	a	30	+	Severe gingivitis	++
Pl	b	3	+	0	+
Do	b	3	0	0	0
Ne	c		++	Anorexia, rhinitis, conjunctivitis, diarrhoea. Euthanized 7 weeks p.i. <sup>3</sup>	+++
So	c		+	Ear mites, slight gingivitis	++
Tr	c		0	Rhinitis, conjunctivitis, keratitis, gingivitis, ear mites	+
Et	d		NT <sup>4</sup>	Dead 7 weeks p.i. after 2 d of depression	+++
Vr	d		0	Episodes of diarrhoea and conjunctivitis	++
Fa	e		+	Ear mites	++
Pa	e		0	0	0
Bi	e		0	0	0

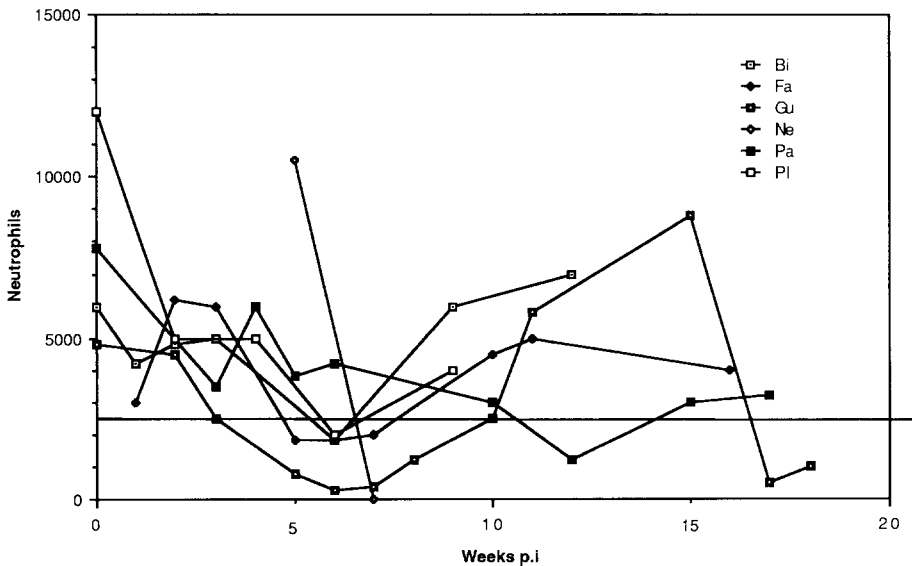
<sup>1</sup>See Table 2<sup>2</sup>Reverse transcriptase activity (cpm × 10<sup>-3</sup>)<sup>3</sup>Post-inoculation<sup>4</sup>No tested



TABLE 5

Leukocyte abnormalities and clinical score of 11 experimental cats

Experimental cats	Leukocytes abnormalities			Clinical score
	Leucopenia	Intensity of neutropenia	Ratio inversion <sup>2</sup>	
Gu	+	+++	+	+++
Ne	+	+++ <sup>1</sup>	+	
Fa	0	++	+	++
Pi	0	0	+	
So	0	0	+	
Ma	0	0	+	+
Pl	0	+	+	
Tr	0	0	+	0
Pa	0	+	+	
Bi	0	+	+	
Do	0	0	0	

<sup>1</sup>Agranulocytosis.<sup>2</sup>Neutrophil-lymphocyte ratio.Fig. 1. Variations in neutrophils counts ( $10^{-3}/\text{mm}^3$ ) in 6 experimentally infected cats.

covered in some weeks and then remained in a stage of asymptomatic seropositivity (with normal haematological values) which has now persisted for 35 months for the earliest experimental infections. It may be noted that in HIV infection, the stage I (primary infection corresponding to seroconver-

sion) is also followed by a stage II of asymptomatic seropositivity (Centers for Disease Control, 1986).

About half the cats (Table 4) developed fever which persisted for about three weeks; although moderate in most cases, fever on occasion reached 40°C and was sometimes recurrent. As shown in Table 4, the intensity of fever and other clinical signs were evaluated by a "clinical score" varying from 0 to +++ (death or severe clinical signs).

A generalised lymphadenitis (hypertrophy or firmer consistency) developed in all the cats at the same time as the clinical disorders and persisted, with some variation in intensity, for several months.

Haematological examination of 11 blood samples revealed the appearance of three transient disorders: neutropenia, lymphopenia and presence of abnormal lymphocytes. Neutropenia was observed in six cats between 4 and 9 weeks p.i. concomitantly with the fever or a few days preceding it. Agranulocytosis associated with a shorter phase of lymphopenia was observed in cat Ne (Table 5 and Fig. 1). An inversion of the neutrophil:lymphocyte ratio was presented by 10/11 cats and only cat Do developed no haematological disorders. The neutropenic phase was associated with the presence in the blood of large mononuclear cells exhibiting basophilic cytoplasm and irregularly shaped round nuclei with loose reticulate chromatin and one or two prominent nucleolus; these atypical lymphocytes were classified as immunoblast-type cells (Fig. 2). A correlation between the number of atypical lymphocytes and the severity of the clinical expression was observed for cat Gu in which the proportion of atypical cells reached 80% of lymphocytes at the peak of each neutropenic episode. It may be noted that the presence of LA associated

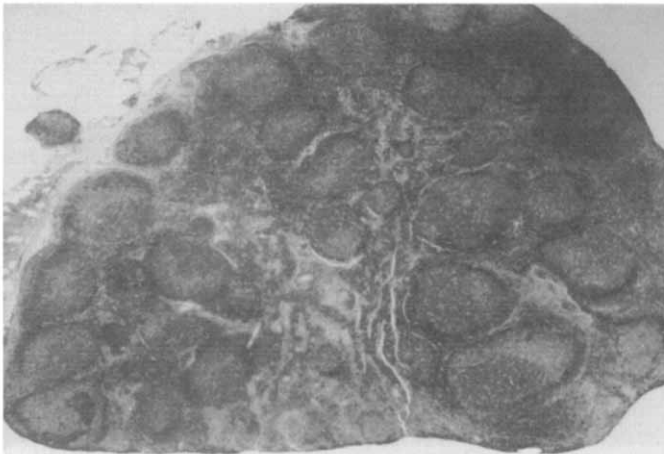


Fig. 2. Atypical lymphocyte seen during the neutropenic phase and classified as immunoblast-type cell (100×12,5).

with atypical lymphoid cells has been reported in man during HIV infection at time of seroconversion (Cooper et al., 1985) and also at the acute stage of infectious mononucleosis (Tursz et al., 1980). The absence of neutrophil counts in several reports concerning the HIV primary infection makes it difficult to establish whether the neutropenia observed in the cat manifests as systematically in the human subject.

Histological examination of the lymph nodes revealed moderate follicular hyperplasia associated with moderate diffuse deep cortical hyperplasia in 2 Ne (7 weeks p.i.) and Gu (12 weeks p.i.). In two cases (cat Fa, 10 weeks p.i. and cat Pl, 11 months p.i.) severe follicular and deep and superficial cortical hyperplasia was observed. The follicles were limited by a thin and sometimes interrupted lymphoid mantle with a very large and active germinal centre which exhibited numerous centrofollicular cells associated with a few immunoblasts. In one of the follicles, a small cluster of mature lymphocytes was observed (Fig. 3). We previously reported a similar appearance in a young cat with generalised lymphadenitis (Deau, 1986). The follicular hyperplasia observed here is altogether comparable to that described in human (Meyer et al., 1984) and simian subjects (Meyer et al., 1985) with acquired immunodeficiency syndromes (AIDS).

In conclusion, clinical signs were observed in 10/13 cats, haematological disorders in 10/12 and LA in all 12 surviving cats. Out of the three clinically normal animals, one developed LA alone, one neutropenia alone and one these two signs together. In other words, an expression of the primary phase of infection (primary infection) was observed in all the experimental animals.

Fever, neutropenia and LA were also observed by Yamamoto et al. (1988)

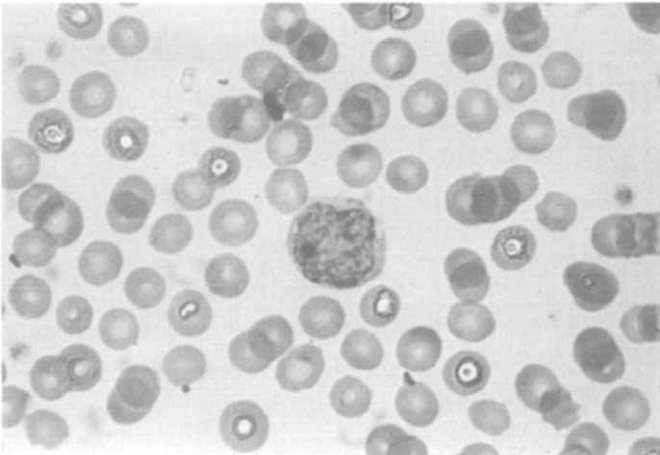


Fig. 3. Histological aspect of a popliteal lymph node resected from Cat Pl, 11 months p.i. (2.5×6,3).

in experimental kittens maintained in isolation after inoculation but these authors did not report anorexia, weight loss and signs of localized infections; while in our experiments the more conventional housing conditions may have constituted an environment more propitious to the clinical expression of neutropenia-related disorders than isolation it is also possible that these differences may have been due to differences in the virulence of the strains used.

The results obtained here with regard to the FIV primary infection invite comparison with the primary stage of HIV infection. In a review of 24 cases, Piette et al. (1987) noted that the most frequent clinical picture consisted of a mononucleosis syndrome with fever (96% of cases), myalgia and arthralgia (79%) and prolonged LA (66% of cases). The proportion of patients presenting a symptomatic initial stage of HIV infection has been evaluated at about 10% (Coulaud and Girard, 1989); since in our study 77% of the cats developed clinical signs, the question may be raised as to whether our observations constitute a faithful reflection of the course of natural feline infection; although it is impossible to answer this question, it should be noted that in our studies the doses used tended, on the whole, to be high and the animals young, and these may both be aggravating factors with regard to the pathogenic effect of the isolates.

In cats inoculated with coculture supernatants, the intensity of the clinical (Table 4) and haematological disorders (Table 5) were proportional to the RT activity ( $\text{cpm} \times 10^{-3}$ ) of the administered dose; the highest dose (210) induced extremely intense reactions (cat Gu), the median doses (30–90) resulted in far more moderate responses (cats Ma and Pi) and the animals receiving the lowest doses (3) developed few or no clinical signs (cats Pl and Do). Thus it is clear that a *dose-effect relation* exists.

### *Seroconversion*

IFA revealed serum antibody titres ranging from 16 to 128 in all the spontaneously and experimentally infected cats. ELISA showed that all of the cats seroconverted on average 24 d after inoculation (Table 6). The rapidity of the serological response seemed to be related to the severity of the primary infection: antibodies appeared 13 and 21 days p.i. in cats Gu and Ne respectively (clinical scores = + + +) and between days 32 and 40 in cat Pa (clinical score = 0). Repeated testing revealed that once the antibodies appeared they remained present for the entire duration of the observation period. All experimental sera tested negative for antibodies to FeSFV by IFA confirming the absence of this virus both in inocula and in recipient cats.

### *Virus recovery from experimental cats*

Attempts to recover the virus from cats at different stages of infection all yielded positive results (Table 3). A CPE similar in nature (syncytial and ballooning cells) and time of appearance (1–4 days) was observed indicating

TABLE 6

Serological results by ELISA of experimental cats using Petaluma strain as antigen

Cat name	Clinical score	Time of sample collection (days p.i.)									
		10	13	14	16	21	26	29	32	35	40
Gu	+++	-		+	+	+	+	+			
Ne		-	-			+					+
Fa	++	-	-				+				
Pi				-			+				
So						-					+
Ma	+		-	-			+				
Pl		-	-						+		+
Tr				-		-					+
Bi	0	-		-	-	-			+		
Do				-					+		
Pa					-		-			-	+

that the *in vitro* biological properties of the isolates have remained unchanged after up to 24 months passage in the cat.

## DISCUSSION

The *in vivo* study conducted here was designed to obtain an acute experimental disease with rapid progression to death that could be used as a relevant animal model for HIV studies. Although in all the experimental animals the transmission was clinically expressed, the clinical signs were transient and the majority recovered in some weeks. The difficulties we encountered here in inducing a rapidly progressing disease illustrates the particular pathogenic properties of the lentiviral subfamily.

Strains Wo and Me isolated here regularly induced CPE within 1–4 days; this interval is, to our knowledge, the shortest published to date. Others strains have been reported to show CPE after 9 days (Harbour et al., 1988), 2–4 weeks (Alexander et al., 1989) and 1–3 months (Ishida et al., 1989); the Petaluma strain isolated from 2 experimentally infected cats induced CPE after 14–21 days and 4–6 weeks (Pedersen, 1987). With regard to RT activity in cocultures, it is accepted that the times to appearance depend on the number of infected cells in the PBMC infected fraction. If it can be taken that the number of infected peripheral lymphocytes during the leucopenic phase preceding seroconversion is about the same for all cats, it would be of interest to compare the *in vitro* properties of different strains isolated at this particular stage of infection. In this condition the RT activity was 0 at day 7 and 5 at day 14 with the Petaluma strain and respectively 120 and 190 in cocultures prepared from cat Gu 2 months p.i. (Table 3). In conclusion, the viruses Wo

and Me isolated from two different cats at the final stage of infection were characterised by a high replication rate and a rapidly induced CPE. The differences in in vitro replication rates between HIV isolates have led investigators to suggest the possibility of the existence of variants. Thus, strains isolated from patients with advanced disease rapidly displayed high RT activity (Asjö, 1986) were able to replicate efficiently and to induce syncytium-formation (Fenyö, 1988). Moreover, high-replicating and syncytium-inducing isolates were associated with a decrease in the number of T4-lymphocytes and a rapid progression to AIDS (Tersmette, 1989). It is generally considered that during the course of human infection pathogenic variants are progressively selected and that they become clearly predominant at the end of the disease. In our work, 3 high-replicating and syncytium-inducing isolates were recovered from cats at the terminal stage of infection with feline AIDS (that is at the most favourable time for isolation of the most highly pathogenic strains). The present data suggest that there may exist a heterogeneity among FIV strains and a relationship between the clinical condition of the donor at the time of isolation and the in vitro growth characteristics of the strain obtained.

In conclusion, the similarities between the pathogenicities of HIV and FIV include the hypothetical progressive selection of variants during the evolution of infection and the clinical expression of the primary infection.

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