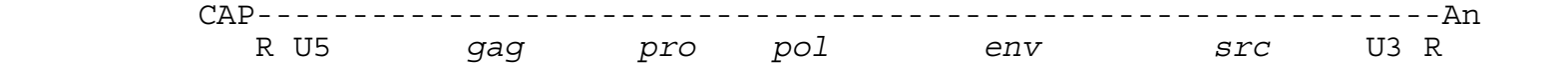
VIROLOGY - MCB 5505

VIRUS FAMILY: **RETROVIRIDAE**

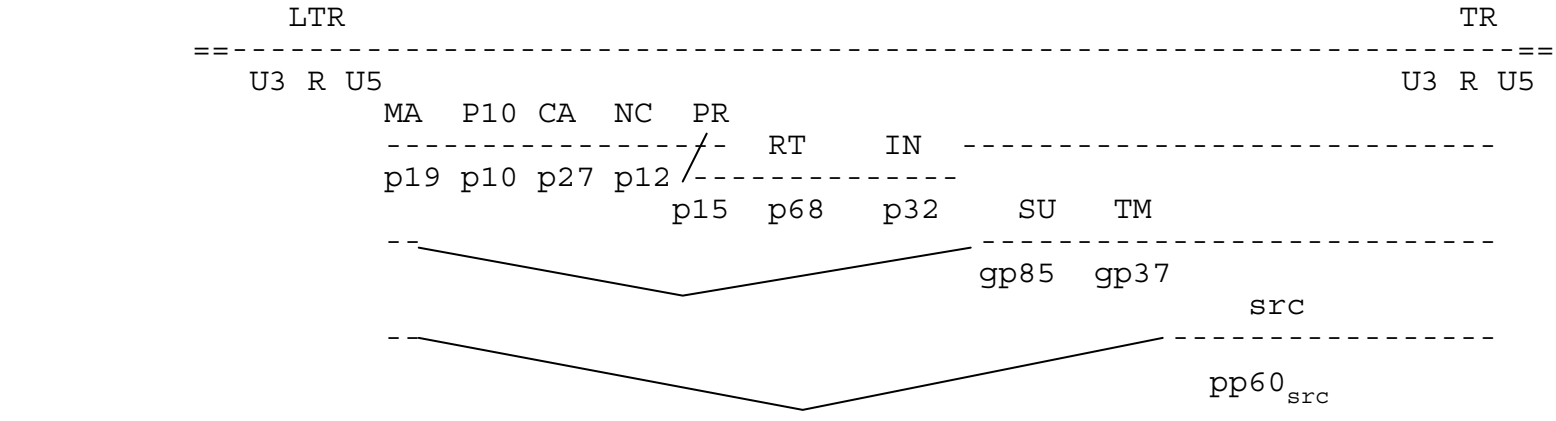
I. DISTINGUISHING CHARACTERISTICS
- A. DIPLOID GENOME OF PLUS-STRAND, mRNA-like RNA
- B. REVERSE TRANSCRIPTASE WITH tRNA PRIMER - UNUSUAL SYNTHESIS OF DOUBLE-STRANDED DNA (GENERATION OF LTRs)
- C. INSERTION OF GENOME (AS DS-DNA) INTO HOST GENOME
- D. CANCER-CAUSING VIRUSES (RNA TUMOR [ONCORNA-] VIRUSES)
- E. IMMUNO-DEFICIENCY VIRUSES (LENTIVIRUSES)

II. STRUCTURE (BASED ON ROUS SARCOMA VIRUS)
- A. SIZE: ABOUT 100 nm IN DIAMETER
- B. ENVELOPE: YES, FROM PLASMA MEMBRANE
  - 1. GLYCOPROTEINS: TWO, DERIVED FROM ENVELOPE POLYPROTEIN (gp120)
    - gp85 (spike or surface, SU)
    - gp37 (transmembrane, TM)
  - 2. MATRIX PROTEIN: p19 (matrix, MA [myristolated])
- C. NUCLEOCAPSID
  - 1. NUCLEIC ACID
    - a. TYPE: RNA BALTIMORE TYPE: VI
    - b. STRANDED: SS
    - c. POLARITY: +
    - d. MOL. WT.:
    - e. # GENES: 10 FROM THREE ORFs
  - 2. GENETIC (PHYSICAL) MAP: (GENBANK AN: NC001407)

GENOME:



PROVIRUS:



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3. CAPSID
   a. SYMMETRY: ??
   b. CAPSOMERS: ??
   c. SIZE:
   d. COMPOSITION
      (1) PROTEINS:

PROTEIN	MW	FUNCTION
	10	??
CA	27	MAJOR CAPSID PROTEIN
NC	12	RNA-BINDING
PR	15	PROTEASE
RT	68	REVERSE TRANSCRIPTASE
IN	32	INSERTASE

III. CLASSIFICATION AND CHARACTERISTIC MEMBERS

GENERA	PROPERTIES	MEMBERS
ALPHARETROVIRUS	AVIAN TYPE C	AVIAN LEUKOSIS V ROUS SARCOMA V
BETARETROVIRUS	MAMMALIAN TYPE B AND D	MOUSE MAMMARY TUMOR V MPMV
GAMMARETROVIRUS	MAMMALIAN TYPE C	MURINE LEUKEMIA V FELINE LEUKEMIA V
DELTARETROVIRUS	BLV/HTLV TYPE	BOVINE LEUKEMIA V PTLV-1
EPSILONRETROVIRUS	PICINE VIRUSES	WALLEYE DERMAL SARCOMA V
LENTIVIRUS	SLOW VIRUSES NON-ONCOGENIC	HIV-1, HIV-2, SIV, VISNA EIAV
SPUMAVIRUS	FOAMY VIRUSES NON-ONCOGENIC	HUMAN SPUMARETROVIRUS FOAMY VIRUSES

IV. VIRAL MULTIPLICATION

A. ABSORPTION. THE VIRUS BINDS TO THE CELL BY INTERACTION OF ITS SPIKE OR SURFACE PROTEIN (SU). THE TM PROTEIN BINDS ANOTHER RECEPTOR AND CAUSES FUSION OF THE VIRAL MEMBRANE WITH THE CELL'S PLASMA MEMBRANE AND PENETRATION OF THE VIRAL CORE INTO THE CYTOPLASM.

B. PENETRATION

C. UNCOATING. THE CORE OR A SUB-CORE IS INVOLVED IN THE SYNTHESIS OF DS-DNA. THE DNA AND SOME PROTEINS ENTER THE NUCLEUS USUALLY DURING MITOSIS WHEN THE NUCLEAR MEMBRANE DISSOLVES.

D. GENOME REPLICATION. THE DS-DNA IS MADE FROM THE GENOMIC RNA USING REVERSE TRANSCRIPTASE (RT) AND tRNA as PRIMER. THE COMPLEX MECHANISM HAS TWO "JUMPS" WHERE THE RT/DNA MOVES FROM ONE PART OF THE TEMPLATE TO ANOTHER WITH THE SAME HOMOLOGY. THE SECOND STRAND IS MADE USING A POLYPURINE TRACK AS PRIMER. LTRs ARE PRODUCED ON BOTH ENDS

OF THE NEW DNA. THE DNA INTEGRATES INTO THE HOST GENOME AT RANDOM A COMPLEX PROCESS CATALYZED BY THE INSERTASE (IN). THE PROVIRUS ALWAYS HAS THE GENE ORDER AS SHOWN ABOVE.
E. GENE EXPRESSION. THE GENOMIC RNA IS TRANSCRIBED FROM THE PROVIRUS. THE U3 REGION OF THE LTR HAS STRONG PROMOTER ACTIVITY. THE TRANSCRIPT STARTS PRECISELY AT THE U3-R JUNCTION. TRANSCRIPTION ENDS WITH POLY-A ADDITION PRECISELY AT THE DOWN STREAM R-U5 JUNCTION. SPLICING USING HOST SPLICEOSOMES PRODUCES SUBGENOMIC RNAs. THE GAG AND GAG-POL POLYPROTEINS ARE MADE FROM THE WHOLE LENGTH (GENOMIC) mRNA. THE ENV PROTEINS, SU AND TM, ARE ALWAYS MADE FROM A SPLICED mRNA. AT THE BEGINNING OF THE SU PROTEIN IS A SIGNAL SEQUENCE THAT DIRECTS THE PROTEIN INTO THE ENDOPLASMIC RETICULUM. SU AND TM ARE GLYCOSYLATED AND DIRECTED TO THE PLASMA MEMBRANE. ACCESSORY PROTEINS AND ONCOGENES ARE ALSO EXPRESSED FROM SPLICED mRNAs.
F. ASSEMBLY. CORES ARE ASSEMBLED BEFORE (OR DURING) BUDDING. THE PROTEASE (PR) CLEAVES THE POLYPROTEINS DURING OR AFTER ASSEMBLY.
G. BUDDING AND/OR RELEASE. BUDDING AND RELEASE OCCURS AT THE PLASMA MEMBRANE. ASSEMBLING CORES INTERACT VIA M PROTEIN WITH TM.

V. CLINICAL CORRELATIONS

ONLY THE PLTV VIRUSES CAUSE NEOPLASMS IN HUMANS. PTLV-1 IS A BLOOD-BORNE VIRUS THAT CAUSES ADULT T-CELL LEUKEMIA.

THE ONCORNAVIRUSES (ALPHARETROVIRUSES – EPSILONRETROVIRUSES) HAVE PROVIDED US WITH A LARGE LIST OF ONCOGENES. FROM *src* TO *ras* THERE ARE ABOUT 100 ONCOGENES THAT HAVE BEEN DISCOVERED IN THE AVIAN AND MAMMALIAN RETROVIRUSES.
TABLE 5.5 IN “STRAUSS AND STRAUSS” PROVIDES A LIST OF RETROVIRAL ONCOGENES CATEGORIZED INTO GROWTH FACTORS, GROWTH-FACTOR RECEPTORS, SIGNAL-TRANSDUCTION KINASES, G-PROTEINS, AND TRANSCRIPTION FACTORS.

THE IMMUNODEFICIENCY VIRUSES CAUSE CHRONIC, PROGRESSIVE DESTRUCTION OF THE IMMUNE SYSTEM. LOSS OF HUMAN T4 CELLS EVENTUALLY RESULTS IN LOSS OF BOTH CELL-MEDIATED AND HUMORAL IMMUNE RESPONSES. DEATH IS DUE TO ONE OF SEVERAL OTHERWISE RARE IMMUNOSUPPRESSIVE DISORDERS (E.G. PNEUMOCYSTIS PNEUMONIA).