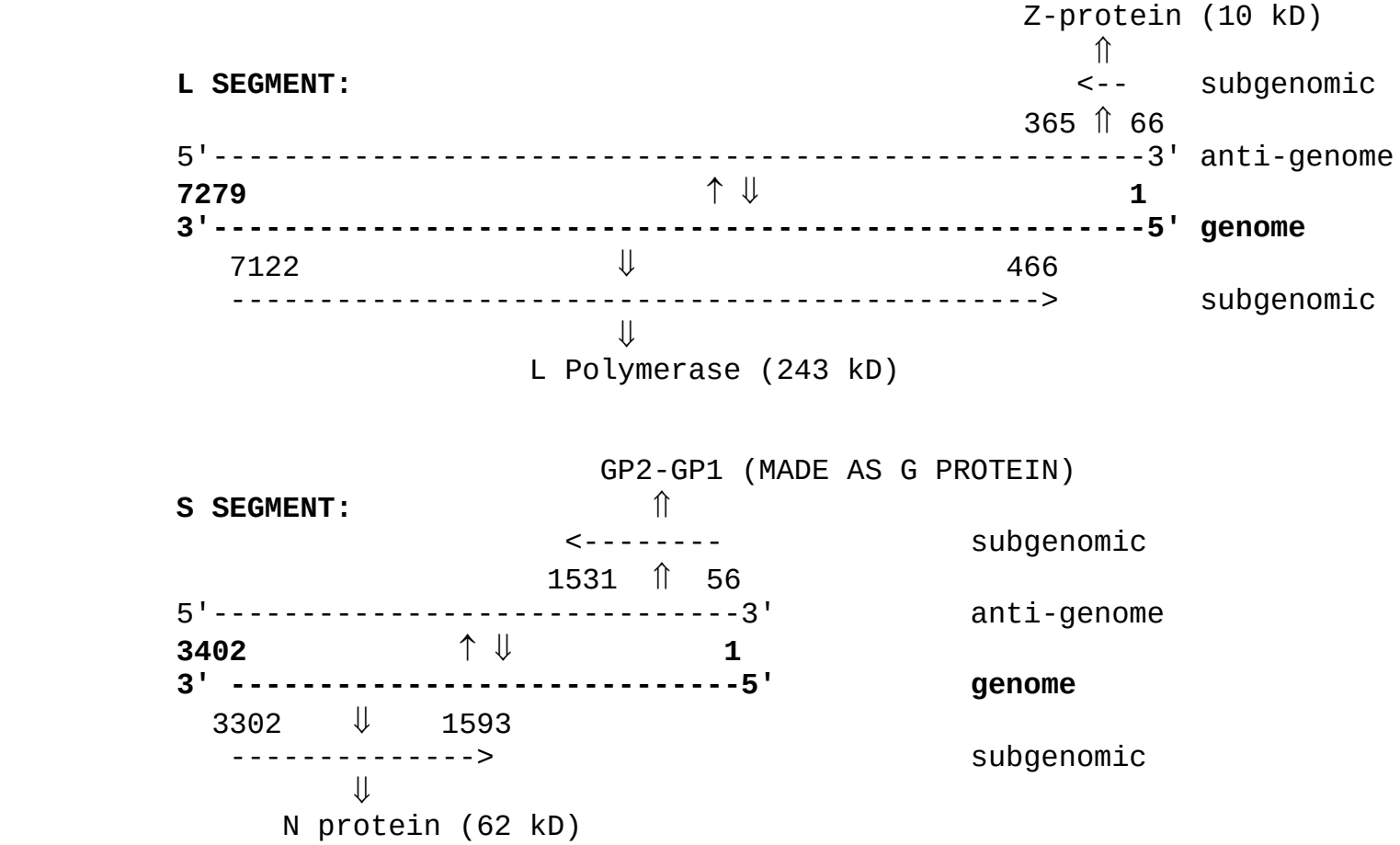
VIROLOGY - MCB 5505

VIRUS FAMILY: **ARENAVIRIDAE** (Arena=sand)

I. DISTINGUISHING CHARACTERISTICS
- A. SPHERICAL, ENVELOPED WITH GLYCOPROTEIN PEPLOMERS
- B. GENOME IN 2 SINGLE-STRANDED, AMBISENSE SEGMENTS
- C. RIBOSOMES PACKAGED INSIDE ENVELOPE (SAND IN EM)
- D. MEMBERS INFECT MAN VIA RODENTS
- E. CAUSE RASH/HEMORRHAGIC-FEVERS
- F. LASSA FEVER V WAS ONE OF THE FIRST "EMERGING VIRUSES"

II. STRUCTURE (BASED ON LASSA VIRUS, JOSIAH STRAIN)
- A. SIZE: 100 - 130 nm in dia.
- B. ENVELOPE: PRESENT - BUDS THROUGH PLASMA MEMBRANE
  1. GLYCOPROTEINS: GP1 (42kD) SPIKE (TETRAMER)
     GP2 (34kD) TRANSMEMBRANE
  2. MATRIX PROTEIN: NONE
- C. NUCLEOCAPSID
  1. NUCLEIC ACID
     - a. TYPE: RNA BALTIMORE TYPE: V
     - b. STRANDED: SS
     - c. POLARITY: AMBISENSE IN BOTH L AND S
     - d. MOL. WT.: L (7279 b) S (3402 b)
     - e. SEQ.-GENBANK AN: L(NC 004297), S(NC 004296)
     - f. # GENES: 5 #ORFS: 2 ON GENOME, 2 ON ANTIGENOME
     - g. TERMINAL BASE-PAIRING REGIONS OF ~20 BP
  2. GENETIC (PHYSICAL) MAP:



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3. CAPSID
   a. SYMMETRY: HELICAL
   b. SIZE: 2 X >100 run
   c. CAPSOMERS: N PROTEIN, 62 KD
   d. COMPOSITION:

PROTEIN	MW (KD)	COPY NO.	FUNCTION
N	62	>1000	NUCLEOPROTEIN
L	243	>10	REPLICASE
Z	10	?	ZN-BINDING PROTEIN (?)

III. CLASSIFICATION AND CHARACTERISTIC MEMBERS

GENERA	PROPERTIES	MEMBERS
ARENAVIRUS	RODENT-RESERVOIRS	LCM IS TYPE VIRUS
	2 SEROGROUPS:	
	OLD WORLD	LASSA, MOBALA
	NEW WORLD	TACARIBE, JUNIN, MACHUPO, PICHINDE

IV. VIRAL MULTIPLICATION

A. **ABSORPTION & PENETRATION:** GP1 protein binds the virus to cell receptor. Endocytosis brings the virus into the cytoplasm and also strips the envelope.

B. **UNCOATING**: Uncoating of the N/RNA is not complete and N protein seems to be required for both "transcription" and RNA replication. Both are catalyzed by protein L.

C. **GENE EXPRESSION:** The virus is ambisense in both its RNA segments, and subgenomic mRNAs are "transcribed from both the genome and the antigenome strands. The first 10 nucleotides plus the cap of host mRNAs are "cannibalized" to provide primers for "transcription" of the two genome segments. L mRNA is transcribed from the 3'-end of the L genomic strand resulting in a large mRNA which is translated into the L-protein. From the 3'-end of the full-length antigenome L strand another subgenomic mRNA is made which codes for the Z-protein. The S RNA genomic strand is also ambisense, and an mRNA (again primed by host-capped nucleotides) is made from its 3'-end and codes for the 62kd N-protein. The antigenome strand is transcribed into another small mRNA that codes for the two Glycoproteins, GP1 and GP2 that are cleaved from a precursor glycoprotein (the G-protein).

D. **GENOME REPLICATION**: The genome is replicated from full-length genome strands which are replicated separately from the mRNA pools. Full-length antigenome strands (vc strands) are made from the genome strand templates. Both reactions are catalyzed by the polymerase, protein L.

E. **ASSEMBLY:** N coats the new viral genomes and they circularize due to their complementary ends (panhandles). The two genome segments (via the N protein ??) interact with the cytosolic domain of GP2, the transmembrane glycoprotein.

F. **BUDDING AND/OR RELEASE:** The two nucleoprotein genome segments aggregate and bud through the plasma membrane. The process is not exact and often multiple copies of the genome and even nearby ribosomes are enclosed in the budding virion. The viral patch is made up of GP2 transmembrane protein bound to a tetrameric, globular GP1 spike protein.

V. CLINICAL CORRELATIONS

A. Lassa fever was first recognized due to an outbreak in Lassa, Nigeria, in 1969. A nurse contracted the disease from a patient in a small hospital and several other hospital workers were also infected. One nurse was evacuated to the US where she recovered, but during the viral isolation at Yale University two others became infected and one died of Lassa Fever. The virus is now known to be endemic in rural West Africa. Its reservoir host is the native mouse, *Mastomys natalensis*. Several outbreaks have occurred since 1969 in both rural and urban settings. All have had disease rates of ~20% and a case mortality rate of ~15%. Millions of West Africans have antibody to the virus, and each year about 2000 die of Lassa Fever.

B. The first known (isolated) Arenavirus was LCM, Lymphocytic Choriomenigitis Virus. This virus infects the common house mouse, *Mus musculus*, without disease, and occasionally infects man. Human infections are often without disease but in some an influenza-like illness develops. Rarely a more serious meningitis or encephalitis is seen.

C. The New World viruses cause three South American hemorrhagic fevers: Argentine (Junin virus), Bolivian (Machupo virus) and Venezuelan (Guanarito virus). All of these diseases are enzootic and man is infected because of close contact with the rodent host. For example the spread of Junin virus to man was probably due to the widespread planting of maize and with it the proliferation of the vole host, *Calomys musculinus*. Symptoms include hemorrhage, thrombocytopenia, leucopenia, hypotension and death results from hypovolemic shock. The most recent outbreak is Venezuelan HF. The virus is enzootic in the cotton rat, *Sigmodon hispidus*. Household contact with rodents seems to be the mode of transmission (due to contaminated urine and droppings).