

USAID

PN ABU 411
93817

CDR Project No. C5-336

Preparation of a Live Vaccine Against the Caprine Arthritis
Encephalitis Virus (CAEV)

FINAL REPORT

DPE-6007

Yaniv Abraham, Ph.D.
Gazit Arnona, Ph.D.
Department of Human Microbiology
Sackler School of Medicine
Tel Aviv University
Tel-Aviv, ISRAEL
FAX. NO. 972/3/642-2275

REC'D IN BOSTON

10/27/95

CC: BOSTON

The objective of the proposed study was to characterize the envelope gene of CAEV and to prepare a vaccine using a vaccinia virus recombinant. The following achievements were obtained:

1. Characterization of the various CAEV molecular clones.

Our first attempt to molecularly clone the CAEV genome from CAEV-infected cells was to use the unintegrated viral genome. Several partial clones were obtained. Since the CAEV full length clone was not infectious we first tried to use these partial clones for constructing the CAEV *env* vaccine. To this end extensive molecular studies were carried out aiming at establishing their genetic structure of these clones. These data showed that all clones were deleted at their 3' end which spans the *env* region. Moreover, data showed that these deleted viral genomes can be packaged into mature viral particles and subsequently we showed that CAEV virus preparations contain defective viral particles. The structure of these clones, and their potential effect in interfering with CAEV productive replication were summarized in our Progress Reports of June 87 - Dec. 87; Jan. 88 - June 88 and July 88 - Dec. 88. The data were published (Gazit et al., 1992).

2. Sequence analysis of the proviral *env* region.

Although the full length clone obtained from the integrated form of CAEV, was not infectious, sequence analysis was performed to reveal whether the *env* region can be used for vaccine preparation. Sequence analysis showed the existence of several premature termination codons inside the *env* region. These data are summarized in Progress Report July 88- Dec. 88.

3. Screening of cDNA libraries for the full length *env* transcripts.

Since the full length CAEV clone contains several stop codons and thus cannot express the viral envelope proteins, the only approach to obtain a biologically potent CAEV *Env* expression vector, was by cloning the CAEV *env* transcripts. First, experiments were performed to establish the pattern of CAEV gene expression. Northern analysis

showed the presence of several multiplied transcripts, in addition to the two known structural transcripts of retroviruses, the full length which encodes the *gag* and *pol* proteins and the *env* which encodes the viral envelope glycoproteins. To isolate the viral transcripts, two CAEV cDNA libraries were constructed from CAEV-infected tahr cells: one library was constructed 8-24 hours after infection and the other one- 48 to 72 hours following infection. The procedure of the preparation and screening of the various transcripts of these libraries are summarized in Progress Reports Jan 89-June 89 and Jan. 90-June 90 and were published (Kalinski et al.,1991).

4. Analysis of the *env* transcript.

Most of the isolated CAEV cDNAs, were established as transcripts encoding the CAEV regulatory proteins, Tat and Rev. Out of 64 clones, only two were established, according to their restriction map, as Env transcripts. The characterization of the regulatory transcripts are summarized in Progress Report Jan. 90- June 90. Detailed nucleotide sequence analysis should be performed to establish the integrity of the *env* transcripts.

5. Characterization of CAEV Peruvian isolates.

In order to enable future construction that will be effective also against CAEV Peruvian isolates, several isolates were provided by our collaborators, and their infectious capability and antigenic cross reactivity with our CAEV variant were analyzed. These data are summarized in Progress Report Jan. 90- June 90.

PUBLICATIONS

1. Kalinski, H., Yaniv, A., Mashiah, P., Miki, T., Tronick, S.R. and Gazit, A. *Virology* 183, 786-792, 1991.
2. Gazit, A., Sarid, R., Mashiah, P., Archambault, D., Dahlberg, J.E., Tronick, S.R. and Yaniv, A. *Virology* 189, 344-349, 1991.