

# FORMULATION AND STABILIZATION OF A RECOMBINANT HUMAN CYTOMEGALOVIRUS VECTOR FOR USE AS A CANDIDATE VACCINE FOR HIV-1

Ozan S. Kumru University of Kansas  
okumru@ku.edu  
Soraia Saleh-Birdjandi, University of Kansas  
Lorena Napolitano, University of Kansas  
Eddy Sayeed, International AIDS Vaccine Initiative  
David Robinson, Robinson Vaccines and Biologics LLC\*  
Sjoerd van den Worm, Oregon Health & Science University  
Klaus Frueh, Oregon Health & Science University  
Sangeeta B. Joshi, University of Kansas  
David B. Volkin, University of Kansas

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Vaccination using Cytomegalovirus (CMV) vectors have recently shown promising results in conferring protection in non-human primates against SIV and Mycobacterium tuberculosis infection (1-3). Since CMV vectors can stimulate the production of high concentrations of systemic effector memory T-cells, CMV vectors (containing the appropriate insert) have the potential to clear SIV/HIV and Mycobacterium tuberculosis infection, provided administration occurs at the onset of infection (1, 3). Despite the promising animal data, CMV vectors are prone to potency loss (i.e., degradation) by freeze-thaw and storage at 2-8°C. In this study, we wished to develop formulations with increased freeze-thaw and liquid stability for a recombinant human CMV vector (rHCMV-1) for use in initial clinical trials including i) reduce vector potency loss to <0.5 log after 1 freeze-thaw cycle and ii) reduce vector potency loss to <0.5 log after 4 hours at 2-8°C storage. To achieve these goals, we screened a library of ~50 pharmaceutical excipients and evaluated their effect on vector potency after 3 freeze-thaw cycles or incubation at 4°C for several days. We found that certain additives completely protected rHCMV-1 against freeze-thaw mediated potency loss. With regards to liquid stability, we found certain additives slowed the rate of rHCMV-1 titer loss when stored at 4°C. After screening various excipient combinations, we evaluated three candidate formulations and benchmarked them against the bulk drug substance (BDS) formulation buffer and another published formulation (4). The candidate formulations were significantly more stable than the formulations used for benchmarking in terms reducing rHCMV-1 titer loss due to freeze-thaw and incubation at 4°C for up to 30 days. Despite providing greater stability than the current BDS formulation buffer, rHCMV-1 titer loss was still observed at 4°C as a function of incubation time, which suggests further stabilization (i.e., lyophilization) is likely necessary for longer term development. This study highlights the utility of empirical design of a liquid formulation of a live viral vector where freeze-thaw and short-term liquid storage are necessary.

## References

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\*Current affiliation: Bill and Melinda Gates Foundation.