

Northeast Structural Genomics Consortium Structural and Functional Studies of Murine Gamma Herpes Virus-68 ORF52

Murine gammaherpesvirus-68 (MHV-68) ORF52 is an abundant, capsid-associated tegument protein. It is well conserved among the gammaherpesviruses, but does not appear to be present in the alpha- and betaherpesviruses. ORF52 is essential for the tegumentation and egress of infectious MHV-68 particles in the cytoplasm. In a collaboration with Dr. Ren Sun at the University of California, Los Angeles and Dr. Hongyu Deng at the Institute of Biophysics, Chinese Academy of Sciences in Beijing, we have carried out structural and functional studies of this important protein. The first results of our studies were published in 2007 (Benach et al., 2007).

As a Community Outreach activity of the NESG, we have determined the crystal structure of ORF52 at 2.1 Å resolution. The structure reveals a dimeric association of this protein, except that the N-terminal α -helix does not obey the symmetry of the dimer (Fig. 1). This helix contains many highly conserved residues, and we hypothesize that it is more likely involved in interactions with other components of the tegument or nucleocapsid of the virus. We have confirmed the self-association of ORF52 by co-immunoprecipitation experiments, and deletion of this N-terminal α -helix abolished the function of ORF52 (Fig. 1). Dr. Deng's laboratory is currently pursuing additional experiments to further elucidate the function of this N-terminal helix as well as the ORF52 protein overall.

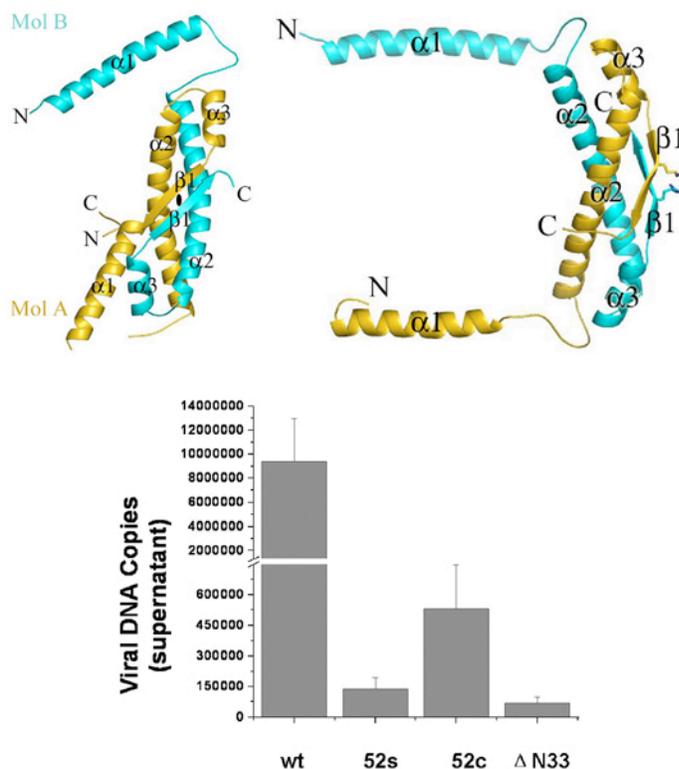


Fig. 1. Structure and function of MHV-68 ORF52. The structure of ORF52 dimer viewed down the two-fold axis (Top left) and from the side (Top right). The N-terminal helix ($\alpha 1$) does not obey the symmetry of the dimer in the crystal (Top left). A model for this helix that obeys the symmetry is shown in the panel at the Top right. Deletion of this helix ($\Delta N33$) abolishes the function of ORF52 (Bottom panel), and the resulting virus is no longer infectious.

Benach, J.; Wang, L.; Chen, Y.; Ho, C.K.; Lee, S.; Seetharaman, J.; Xiao, R.; Acton, T.B.; Montelione, G.T.; Deng, H.; Sun, R.; Tong, L. *J. Biol. Chem.* 2007, 43: 31534 - 31541. Structural and functional studies of the abundant tegument protein ORF52 from murine gammaherpesvirus-68.