

## Investigation of homo-oligomeric interface and binding hotspot of Latent membrane protein-1 (LMP-1) of Epstein-Barr virus (EBV)

<sup>1</sup>Guin Lee, <sup>2</sup>Deanne W. Sammond, <sup>2</sup>Catherine Joce, <sup>3</sup>Ryan Takeshita, <sup>3</sup>Sarah E. McQuate, <sup>3</sup>Nilanjan Ghosh, <sup>3</sup>Jennifer M. Martin, <sup>2</sup>Xiaohui Wang, <sup>2</sup>Tina X. Zhao, <sup>2</sup>Jonel P. Saludes, <sup>2</sup>Adam Csakai, <sup>2</sup>Zeno Fiorini, <sup>2</sup>Sherry A. Chavez, <sup>4</sup>Jing Li, <sup>5</sup>Krisztina Varga, and <sup>2</sup>Hang Yin

<sup>1</sup>Department of Chemistry, Pennsylvania State University, Abington, PA 19001, USA

<sup>2</sup>Department of Chemistry and Biochemistry, University of Colorado, Boulder, CO 80309

<sup>3</sup>Department of Molecular, Cellular, Developmental Biology, University of Colorado, Boulder, CO 80309

<sup>4</sup>Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, 100032, China

<sup>5</sup>Department of Chemistry, University of Wyoming, Laramie, WY 82071, USA(ltg10@psu.edu)

---

A human herpesvirus, Epstein-Barr virus (EBV), establishes lifelong infection through memory B cells and often leads to lymphoid malignancies and lymphoproliferative syndromes. Although the detailed mechanism of LMP-1 activity is not clearly known, previous studies indicate that EBV uses the viral latent membrane protein 1 (LMP-1) for B lymphocyte immortalization. Our study demonstrates the fifth transmembrane helix (TM5) of LMP-1 form homotrimeric complexes. The polar aspartic acid residue (D150) of TM5 embedded in the membrane mediates the self-association of TM5. *In vivo* and *in vitro* studies indicate that the trimerization of TM5 plays a key role in constitutive activation of signaling of LMP-1. In addition, we developed small molecule inhibitors specifically disrupting the TM5 trimerization, suggesting a new strategy for drug development targeting transmembrane protein-protein interactions.

### References

1. Li, H. P., and Chang, Y. S. J Biomed Sci 2003, 10, 490-504.
2. Offen, W. F., III, Geiger, T. R., and Martin, J. M. J Virol 2003, 77, 3749-3758.