BS69 Specifically Scaffolds Latent Membrane Protein 1 and TRAF6 to Activate the JNK and NF-κB Pathways

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We previously demonstrated that the Epstein-Barr virus-encoded latent membrane protein 1 (LMP1) potently activates the cellular JNK pathway by sequentially engaging an unknown adaptor, TRAF6, TAB1/TAK1, and JNKK1/2 (Wan et al., 2004). We now provide evidence showing that BS69, a MYND domain-containing cellular protein, is the adaptor that bridges LMP1 and TRAF6. BS69 directly interacts with both LMP1 and TRAF6 in yeast and in mammalian cells. While LMP1 promotes the binding of BS69 to TRAF6, the complex formation between LMP1 and TRAF6 is BS69-dependent. Importantly, knockdown of BS69 by siRNA specifically inhibits activation of both JNK and NF-κB by LMP1 but not by tumor necrosis factor α or interleukin-1β. Thus, BS69 is the key adaptor mediating the stimulatory effect of LMP1 on JNK and NF-κB, which may contribute to EBV-mediated cell transformation.

Reference:

Jun Wan, Luguo Sun, Jennifer W. Mendoza, Yiu Loon Chui, Dolly P Huang, Zhijian J. Chen, Nobutaka Suzuki, Shinobu Suzuki, Wen-Chen Yeh, Shizuo Akira, Kunihiro Matsumoto, Zheng-gang Liu, and **Zhenguo Wu** (2004). Elucidation of the JNK pathway mediated by Epstein-Barr virus encoded latent membrane protein 1. *Mol. Cell Biol.* **24**: 192-199.