S2-2

Activation of Non-canonical NF-κB Pathway Mediated by STP-A11, an Oncoprotein of *Herpesvirus saimiri*

Young-Hwa Chung

Department of Nanomedical Engineering, Joint-Research Center of Pusan National University-Fraunhofer IGB, BK21 Nanofusion Technology Team, Pusan National University

Although STP-A11, an oncoprotein of *Herpesvirus saimiri*, has been known to activate NF-κB signaling pathway, the detailed mechanism has not been reported yet. We herein report that STP-A11 activates non-canonical NF-κB pathway, resulting in p100 processing to p52 (Fig. 1).

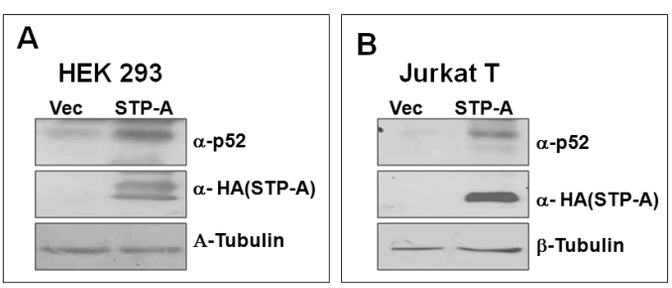

Fig. 1. Induction of NF-κB2, (p52) production by expression of STP-A11.

In addition, translocation of p52 protein (NF-κB2) into the nucleus is observed by the expression of STP-A11 (Fig. 2).

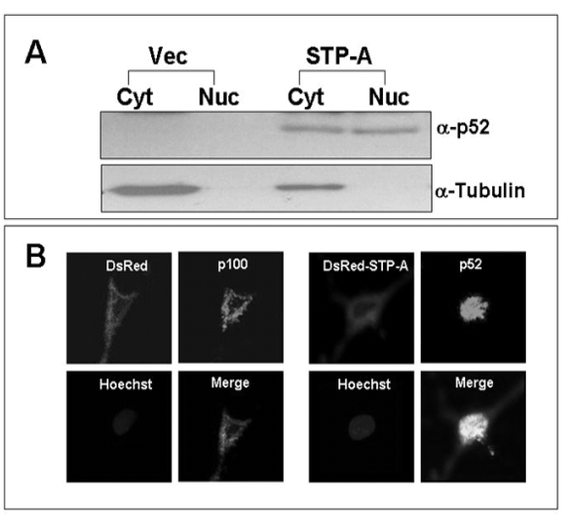

Fig. 2. Translocation of p52 protein into the nucleus by the expression of STP-A11.

And NIK is involved in p100 processing by the expression of STP-A11 (Fig. 3).

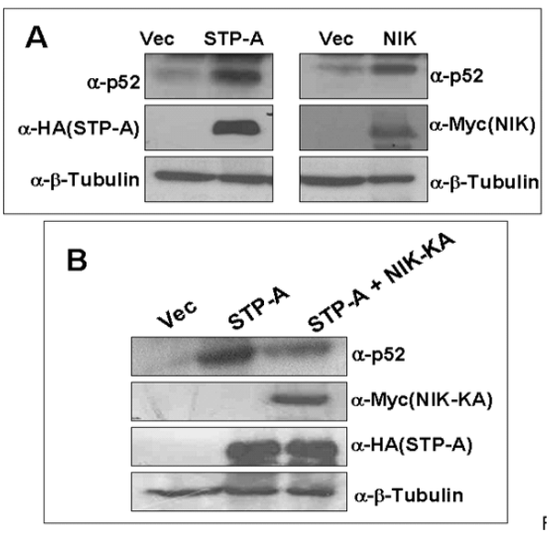

Fig. 3. Partial involvement of NIK in NF-κB2 production mediated by STP-A11.

STP-A11-mediated processing of p100 to p52 protein requires proteosome-mediated proteolysis since MG132 treatment clearly blocked p52 production in spite of the expression of STP-A11 (Fig. 4).

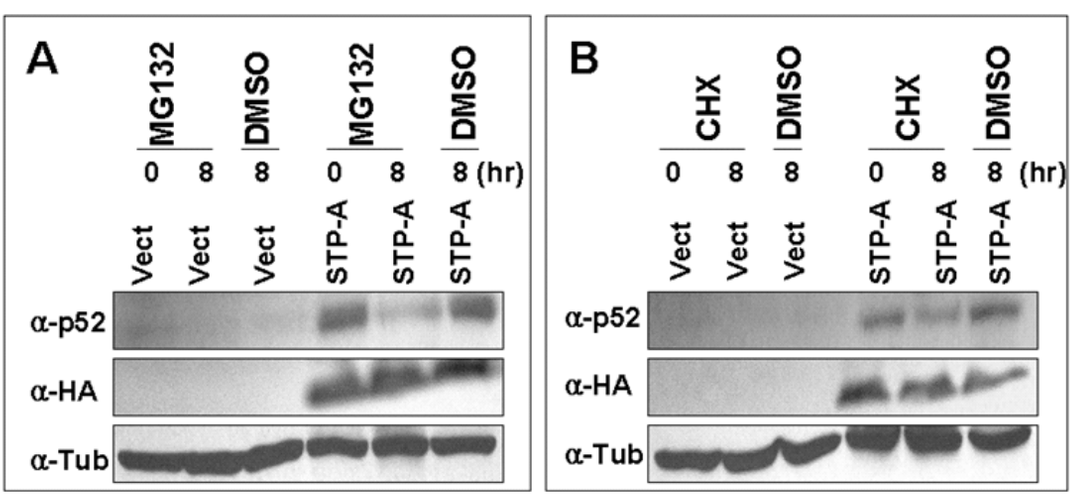

Fig. 4. Proteosome-mediated p100 processing to p52 by the expression of STP-A11

Analysis of STP-A11 mutants to activate NF-κB2 pathway discloses the requirement of TRAF6-binding site not Src-binding site for STP-A11-mediated NF-κB2 pathway (Fig. 5)

Blockage of p52 production induced by expression of STP-A11 using siRNA against p52 enhanced a chemotherapeutic drug - mediated cell death, suggesting that p52 production induced by the expression of STP-A11 would contribute to cellular transformation, which results from a resistance to cell death (Fig. 6).

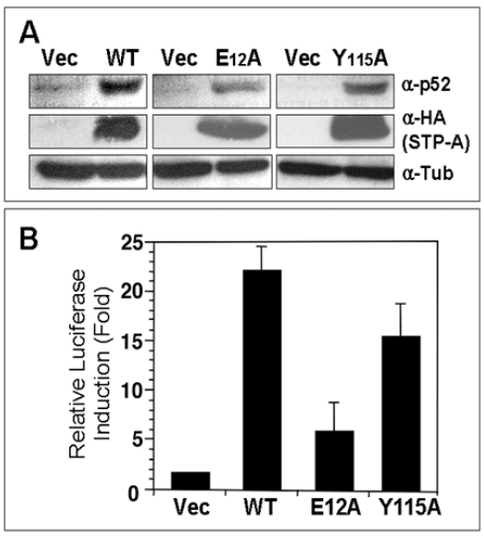

Fig. 5. Requirement of TRAF6-binding site for STP-A11-mediated p100 processing but not Src-binding site.

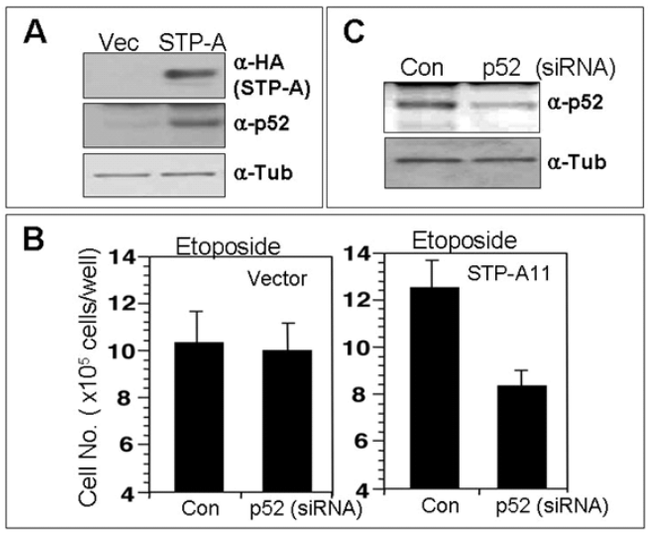

Fig. 6. Enhancement of a drug-induced cell death by suppression of STP-A11-mediated p52 production using siRNA against p52.