

SNAIL MUCUS INCREASES THE ANTI-CANCER ACTIVITY OF ANTI-PD-L1 ANTIBODY IN MELANOMABo-Rong Chen, Wei-Chien Huang*. *China Medical University, Taichung, Taiwan*

Background Malignant melanoma is the most aggressive disease of skin cancer and associated with high-levels of morbidity, mortality, and therapy resistance. The interaction between transmembrane proteins programmed cell death protein 1 (PD-1) and PD-L1 has been found to inhibit the anti-tumor immune response. Disruption of the PD-1/PD-L1 interaction with monoclonal antibodies has been developed as a breakthrough therapeutic strategy in malignant melanoma, but the effective rate is limited. New advances in pharmaceutical strategies are required for sensitizing immune checkpoint inhibitors. Snail mucus has showed its abilities of anti-inflammation, anti-angiogenesis, and anti-cancer activity. The effects of snail mucus on PD-L1 level in melanoma and anti-cancer activity of anti-PD-1 antibody were investigated in this study.

Methods Cell viability and apoptosis of melanoma cell lines were determined in MTT and flow cytometry analyses. Gene expressions were measured in RT-qPCR and Western blot analyses. The cellular cytotoxicity of CD8⁺ on melanoma cells in co-culture system was determined in flow cytometry analysis. Statistical significance was analyzed by using the t-test. P-values < 0.05 are considered statistically significant.

Results Treatments with snail mucus suppressed cell proliferation of various cutaneous melanoma cells. Snail mucus increased sub-G1 population, DNA fragmentation and apoptotic cell death, accompanied with the induction of caspase 3 and PARP cleavages, in A375 cutaneous melanoma cells. The increases in protein expressions of Fas signaling suggested the involvement of extrinsic apoptosis pathway in snail mucus-induced cell death. PD-L1 expression was upregulated in the snail mucus-treated A375 cells, and co-treatment with Atezolizumab anti-PD-L1 antibody and snail mucus showed synergistic cytotoxicity of A375 cells in the presence of CD8⁺ T cells.

Conclusions Snail mucus alone induced both extrinsic apoptotic cell death and PD-L1 expression in cutaneous melanoma cells. Co-treatment of snail mucus and anti-PD-L1 antibody showed the enhanced anti-cancer activity for this disease. Snail mucus could be used as a promising therapeutic to promote the anti-cancer activity of immune checkpoint inhibitors.

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