1. **No.**

   FP01901015

2. **Title**

   Effects of Nicotine on Immune Checkpoint Blockade Associated Molecules in Human Anti-cancer Immunotherapy

3. **Period**

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4. **Summary**

   The immune checkpoint molecules (PD-L1 and PD-L2) have a substantial contribution to Anti-tumor immunotherapy including breast cancer. Breast cancer have 3 subtypes (Luminal-type, HER2-type and Triple-negative breast cancer-type) defined as an expression profile of receptor with estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 (HER). In this study, we focused on the effect of nicotine signaling for regulation of PD-L1 and PD-L2 expression on breast cancer cell lines. We hound that expression levels of PD-L1 and PD-L2 were different in 3 subtype. These molecules highly expressed on poor-prognosis breast cancer cell line (triple-negative breast cancer-type; HCC1937, MDA-MB-231), moderately expressed on medium degree-prognosis breast cancer cell line (HER2-type; SK-BR-3) and poorly expressed on good-prognosis breast cancer cell lines (Luminal-type; MDA-MB-361, MCF7). Nicotine treatment decreased PD-L1 and PD-L2 expression on SK-BR-3, but not on triple-negative breast cancer-type cell lines. PD-L1 and PD-L2 expression regulated by phosphorylation of Akt. We hound that nicotine decreased Akt phosphorylation. These results suggested that nicotine treatment regulates immune checkpoint molecules, PD-L1 and PD-L2 expression via inhibition of Akt phosphorylation. In fact, the therapeutic agent targeted Akt is already developed for breast cancer treatment. Nicotine signaling may be good therapeutic target.