Jeong Hwa Park et al., Arch Cancer Res 2018, Volume 6
DOI: 10.21767/2254-6081-C4-015



## A novel innate immune checkpoint inhibitor protein in tumor microenvironment

**Jeong Hwa Park**[1], **Yeong-Min Park**[1] and **Tae Heung Kang**[1]
[1]Konkuk University, South Korea

After cancer treatment using chemotherapy and radiotherapy, tumor microenvironment continually occurs inflammation, which depend on damage-associated molecular pattern (DAMPs) released from apoptotic tumor cells. In this case, tumor microenvironment is regarded as inflammation zone and induce various immune cells infiltration, pro- and anti-inflammatory cytokines production and interaction between immune cells and cancer cells. These, a dynamic and complex microenvironment induce a favorable state for tumor growth. Thus, recent studies assert that it is important to regulate excessively increased inflammatory response in the tumor microenvironment accordingly. Annexin V is a $Ca^{2+}$-dependent phospholipid binding pro¬tein and known to bind to exposed phosphatidylserine on the apoptotic cells. Several groups and our study have recently demonstrated that annexin V has anti-inflammatory effects by inhibiting bone-marrow derived dendritic cell (BMDCs) activation and pro-inflammtory cytokine production. So, we suggest that Annexin V as a therapeutic approach for controlling inflammatory response in cancer patients having increased inflammation in tumor microenvironment. Therapeutic efficacy was demostrated activation of tumor-specific $CD^{8+}$ T cells ($P < 0.001$), inhibition of tumor growth ($P < 0.05$) and increase of survival ($P < 0.05$) in tumor bearing mouse compared to control. AnnexinV protein administration was decreased significantly TGF-beta 1 cytokine production ($P < 0.001$) and immunosuppressive cells infiltration ($P < 0.001$) in tumor microenviroment compared to non-treated group. We identified another role of Annexin V protein, which has capacity of apoptotic tumor cell target, as an innate immune check point inhibitor in tumor microenvironment. This results could primarily pave the road for the development of anti-tumor immunotherapy.

junghwa0814@hanmail.net

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