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Monoclonal antibody immunotherapy of human triple negative breast cancer (TNBC) growth by targeting ANX A2: A potential therapeutic target

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ANX A2 is a major cell surface receptor for fibrinolytic protein tissue plasminogen activator (tPA). So far, clinical and experimental studies found strong association of ANX A2 expression with aggressive and metastatic phenotype of human cancers and correlated with poor prognosis and overall survival (OS). For the first time, we discovered specific expression of ANX A2 in human TNBC cell lines. Minimal or no ANX A2 expression was detected in non-invasive ER positive breast cancer cell lines suggesting an association of ANX A2 with aggressive phenotype of breast cancer. Our *in vitro* studies demonstrated that ANX A2 dependent plasminogen activation plays a major role in breast cancer invasion, neoangiogenesis and tumor growth. We demonstrated that anti-ANX A2 immunoneutralization of ANX A2 inhibited human xenograft TNBC growth in nude mice confirming critical role of ANX A2 in breast tumor growth. Moreover, nude mice pretreated with anti-ANX A2 followed by implantation of TNBC cells demonstrated complete rejection of tumor growth when monitored up to100 days. These data provide strong evidence that ANX A2 plays an important role to establish cross-talk between tumor and stromal cells to build favorable environment for tumor cells to prepare for growth and invasion. Analysis of tumor tissue demonstrated that anti-ANXA2 mAb treatment caused significant inhibition of plasmin generation and inhibited activation of matrix metalloproteinase (MMP-9 and MMP-2) enzyme system in the tumor microenvironment. Taken together, these data suggest that ANX A2 may represent a new target for the development of therapeutics for treatment/prevention of aggressive TNBC.