Role of annexin A1 in the dynamics of macrophage polarization in the breast tumor microenvironment

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Tumor-associated Macrophages (TAMs) choreograph various aspects of the tumor microenvironment. Annexin A1 (ANXA1) is an anti-inflammatory protein is highly expressed in metastatic breast cancer. Gene Expression Omnibus (GEO) and array express was used to assess the association between TAMs and breast cancer in the patients. MMTV-Wnt1 mouse model was used for in vivo study. Microarray Affymetrix was done to find the signaling mechanism involved. LC-MS was done to find the array of secreted protein by the breast cancer cells. Clinically, we found that M2 TAMs were highly enriched in Claudin-low breast cancer subtype and was strongly associated with ANXA1 gene expression, which was validated in our mouse model. Additionally, macrophages were skewed to a more M2 TAM-like phenotype upon co-culture with breast cancer cells, with enhanced migratory and invasive properties and phagocytic potential, which was reduced in the ANXA1-/macrophages. TAMs isolated from the breast tumors of wild type and ANXA1 knockout mice wherein 4T1 had been injected orthotopically, showed higher percentage of M2 macrophages in the wild type as compared to the ANXA1 KO. We have found a novel signaling loop connecting RANTES-Annexin A1-stat3-Arginase 1 using our Affymetrix and LC-MS data, which has been also validated in our ex vivo and in vivo model. This study demonstrates a novel role of ANXA1 in regulating the dynamic process of macrophage polarization in the breast tumor microenvironment and future studies include abrogating this process using a novel stat3 inhibitor.

Biography
Shreya Kar is an Industrious Researcher with the President’s Graduate Fellowship at the National University of Singapore (NUS). She has published six research articles in peer-reviewed journals. She is the student Ambassador currently at EACR and PSS. She has completed her master’s degree in Biotechnology from Calcutta University, India with a Gold medal.

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