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Novel antibody for cancer immunotherapy: Beyond and synergistic with immune checkpoint blockade therapy

During tumorigenesis, human cells were induced to express a family of MHC I-chain related molecules A and B (MICA and MICB, generally termed MIC) on the surface which serve as the ligands for the activating immune receptor NKG2D expressed by all human NK, CD8 T, NKT and subsets of γδ T cells. Theoretically, engagement of NKG2D by tumor cell surface MIC deemed to signal and provoke the immune system to eliminate transformed cells. Clinically, almost all advanced tumors in cancer patients produce soluble MIC through proteolytic shedding mediated by metalloproteases, or by release in exosomes derived from the cell membrane. Tumor-derived sMIC is known to be highly immune suppressive and profoundly insults the immune system by downregulating receptor NKG2D expression on effector NK and T cells, driving the expansion of tumor-favoring myeloid suppression cells, skewing macrophages into alternatively activated phenotypes and perturbing NK cell peripheral maintenance. High levels of serum sMIC significantly correlate with advanced diseases of many types of cancer. These observations clearly endorse sMIC to be a cancer immune therapeutic target. However, due to mice lack homologues to human MIC, this concept was not proven until our recent studies. Using a "humanized" MIC-transgenic spontaneous mouse model which recapitulates the NKG2D-mediated onco-immune dynamics of human cancer patients, we show that neutralizing circulating sMIC with a first-in-field monoclonal antibody B10G5 alleviates the immune suppressive effect of sMIC and revamps endogenous anti-tumor immune responses. Therapy with B10G5 results in effective debulking of primary tumor and elimination of metastasis, with no observed toxicity. Furthermore, we show that clearing sMIC with B10G5 also enhanced the efficacy of other cancer immunotherapeutic modalities, such as immune checkpoint blockade or adoptive cell-based therapy pre-clinically. Our study has launched a new avenue of cancer immunotherapy which can be readily translated into clinical trials.

Speaker Biography

Jennifer Wu joined Northwestern University in August 2017 as a tenured Professor in Urology. Dr. Wu previously served as a Professor of Microbiology and Immunology at the Medical University of South Carolina and the University of Washington. Dr. Wu obtained her PhD from the University of British Columbia in Canada followed by post-doctoral training in Fred Hutchinson Cancer Research Center (FHCRC) and faculty position at the University of Washington. Dr. Jennifer Wu's research focuses on understanding how cancer cells edit the immune system with the ultimate goal to develop effective immune therapy to control cancers.

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