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MS17-38 mAb targeting of PODXL-v2 inhibits gastric cancer growth and metastasis

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Gastric cancer is the primary cause of cancer-specific mortality worldwide. PODXL (podocalyxin-like protein or podocalyxin) is a cell-surface glycoprotein that belongs to CD34 family of sialomucins. PODXL-v1 is widely expressed on vascular endothelium, mesothelial cells, and platelets; in contrast, PODXL-v2, a truncated short form of PODXL is specifically expressed or up-regulated in numerous cancer cell types as well as in small blood vessels in tumor tissues. There remains considerable interest in generating monoclonal antibodies (mAbs) directed against specific tumor targets for antigen (Ag) discovery, diagnosis and therapy. MS17-38 mAb was generated by live cells HTS and was demonstrated to bind to a specific conformational epitope of PODXL-v2 on GC cells. PODXL-v2 expression inhibition by PODXL-v2 siRNA or the PODXL-v2-neutralizing antibody MS17-38 resulted in inhibition of GC cell growth and prevention of GC cell migration in vitro. Furthermore, in vivo studies demonstrated that MS17-38 mAb can potently inhibit tumor growth and prevent MKN-45 metastasis to the lungs in nu/nu mouse models. Finally, high expression of PODXL-v2 was associated with advanced GC stage and short survival time ($P<0.01$). Additional engineering of this mAb into chimeric or humanized forms could permit development of MS17-38 for diagnosis, staging or therapy of human malignancy. Our findings indicate that PODXL-v2 is specifically expressed in the extracellular matrix of GC, and MS17-38 mAb directed against a conformational epitope of PODXL-v2 identified through HTS can functionally inhibit GC cancer cell growth and migration/metastasis both in vitro and in vivo. MS17-38 is a promising functional antibody directed against GC that could potentially be developed into a therapeutic mAb for clinical application.

Biography:

Dr. Zhang Dong-qing is a professor in the Department of Microbiology and Immunology, Shanghai Institute of Immunology, Shanghai Jiao Tong University School of Medicine, China. He graduated from Shanghai Second Medical University in 1985 majoring in medicine. Then he obtained the Master Degree in Shanghai Institute of Immunology, Shanghai Second Medical University in 1991. He worked on research as a postdoctoral fellow in the Department of Nerve immunology research institute McGill University from 1997 to 1998; Also, in 2005 he studied in Yale University School of Medicine, as a visiting professor.