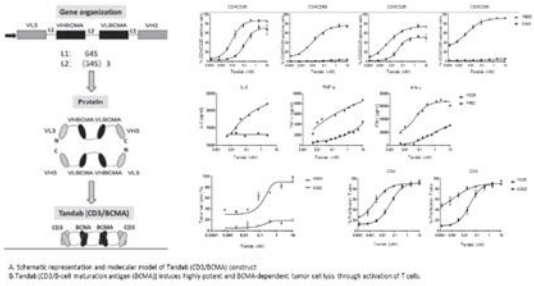
A Novel CD3/BCMA Bispecific T-cell Redirecting Antibody Treatment for Multiple Myeloma

Yanjun Zhang,M.D. State Key Laboratory of Experimental Hematology,China

Abstract (300 word limit)

Multiple myeloma (MM) is a B-cell malignancy for which new treatments are urgently needed. Redirecting the activity of T cells by bispecific antibodies against tumor cells is a potent approach. The B-cell maturation antigen (BCMA) is a highly plasma cell-selective protein and therefore is an ideal therapeutic target for T-cell redirecting therapies. The main objective of this work is to target the BCMA by generating BCMA-specific murine monoclonal antibody and construct a cluster of differentiation 3 (CD3)/BCMA-directed tandem diabodies (Tandab). In brief, using standard hybridoma technology, we developed a novel BCMA specific monoclonal antibody, that specifically bind with BCMA+ cell lines and MM patient sample; whereas BCMA-cells were not recognized. For T cells by bispecific antibodies application, we constructed a Tandab (CD3/BCMA) simultaneously targeting both CD3 and BCMA and our studies demonstrated that Tandab (CD3/BCMA) was functional with specific binding capability both for CD3+ cells and BCMA+ cells. It induced selective, dose-dependent lysis of BCMA+ cell lines, activation of Tcells, release of cytokines and T-cell proliferation; whereas BCMA−cells were not affected. Furthermore, we demonstrated that Tandab activity correlates with BCMA expression, with higher potency observed in highly BCMA expressing tumor cells. In vivo, the purified Tandab (CD3/BCMA) significantly inhibited the tumor growth in a subcutaneous NCI-H929 xenograft model. Taken together, these results show that the Tandab (CD3/BCMA) displays potent and selective anti-MM activities and represents a promising immunotherapeutic for the treatment of MM, even in the CAR-T cells.

Image



Recent Publications (minimum 5)

1.A Noel CD3/BCMA Bispecific T-cell Redirecting Antibody for the Treatment of Multiple Myeloma.J Immunothe.2021.
2.A Noel Blockade CD47 Antibody With Therapeutic Potential for Cancer. Frontiers in Oncology, 10:1-10.
3.Bispcific CD3-HAC carried by E1Aengineered mesenchymal stromal cells against metastatic breast cancer by blocking PD-L1 and activating T cells. Journal of Hematology & Oncology 2019,12:46.
4.Mesenchymal stromal cells as vehicles of tetravalent bispecific Tandab（CD3/CD19) for the treatment of B cell lymphoma combined with IDO pathway inhibitor D-1-methyl-tryptophan. Journal of Hematology & Oncology,2017 Feb 23;10(1):56.
5.Surface expression of anti-CD3scfv stimulates locoregional immunotherapy against hepatocellular carcinoma depending on the E1A-engineered human umbilical cord mesenchymal stem cells. Int. J. Cancer: 141, 1445–1457



Biography (150 word limit)

Yanjun zhang, Associate Professor of molecular pharmacology, State Key Laboratory of Experimental Hematology, Institute of He matology & Hospital of Blood Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College, grew up in China and received her Bachelor's degree from the University of China Medical in 2001. After she obtained her M.D. degree from the Peking Union Medical College in 2011, she joined Professor Dongsheng xiong's Lab as an assistant professor. In the meantime, she started her research on target immunotherapy. Yanjun zhang was promoted to Associate Professor at State Key Lab oratory of Experimental Hematology in 2016 and went to University of California, Los Angelas as a visting scholar in 2019. He did a lot work on overcoming multi-drug resistant and applicated her results into many local hospital, which won the 2013 3rd award of TIANJIN nature science. Recently, she focus on the diabody and established a novel antibody delivery system to tumor environment. Many achievements had been published on the top journals:<biomaterials>, <international of hematology & oncology>, <cancer letter>.

Email: zhangyanjun@ihcams.ac.cn

Notes/Comments:

Presenting author details

Full name: Yanjun Zhang
Contact number: +1-2135779636
Twitter account:
Linked In account:
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