Lu Wen et al., Immunotherapy (Los Angel) 2017 (Suppl)
DOI: 10.4172/2471-9552-C1-005

Adoptively transferred B cells directly kill tumor cells via the CXCR4/CXCL12 and perforin pathways

Lu Wen[1], Qiao Li[1], Leiming Xia[1], Yang Xia[2], Queening Chen[2], Yi Wang[2], Xiang Sun[2], Yangyi Bao[3], Steven K Lundy[3], Fu Dai[3] and **Alfred E Chang[3]**
[1]University of Michigan Medical School, USA
[2]The First People's Hospital of Hefei, China
[3]Huazhong University of Science and Technology, China

Over the years, the role of B cells in the host immune response to malignancy has been overshadowed by our focus on T cells. The role played by B cells in cancer immunology is complex and controversial. The observation made by our lab that activated B cells alone can mediate tumor regression in the adoptive immunotherapy of solid tumors is innovative. One novel mechanism by which activated B cells mediate tumor regression is via direct tumor cell cytotoxicity in the absence of antibodies. We reported that antitumor B cells directly kill tumor cells via the Fas/FasL pathway and are regulated by IL-10. In this study, we defined additional mechanisms involved in B cell antitumor immunity. Administration of IL-2 significantly augmented the therapeutic efficacy of adoptively transferred tumor-draining lymph node (TDLN) B cells which express IL-2R. Furthermore, we detected CXCR4 expression on 4T1 TDLN B cells and 4T1 tumor cells produced its ligand CXCL12. Transwell experiments demonstrated the chemotraction of CXCR4-expressing 4T1 TDLN B cells towards CXCL12-producing 4T1 cells. Blockade of CXCR4 using a CXCR4-specific inhibitor, AMD3100, significantly reduced the killing of 4T1 tumor cells by 4T1 TDLN B cells. Blockade of FasL and CXCR4 concurrently inhibited B cell-mediated direct killing of tumor cells in an additive manner, indicating that both Fas/FasL and CXCL12/CXCR4 pathways are involved in the direct killing of 4T1 cells by 4T1 TDLN B cells. TDLN B cells produced perforin. Additional experiments showed that effector B cells could directly kill tumor cells via the Fas/FasL and CXCR4/CXCL12 pathways as well as perforin. These findings underscore the diversity of function by which B cells can play an important role in the host immune response to tumor and clearly indicated that transferred effector B cells can act independently of T cells in causing tumor destruction in adoptive immunotherapy.

Biography

Qiao Li has significant expertise in tumor immunology and cancer immunotherapy since last 15 years. His laboratory research interests focus on the development of cancer immunotherapy using immune cells, such as T cells, B cells and dendritic cells (DCs). Specifically, application of anti-tumor B cells, and generation of DC-based cancer stem cell (CSC) vaccines to target cancer stem cells represent novel directions in cancer immunotherapy. Administration of DC-CSC vaccine targeting CSCs inhibited local tumor recurrence, reduced spontaneous lung metastasis, and prolonged animal survival. Mechanistically, his novel CSC vaccination strategy conferred host both antibody responses and CTL functions against cancer stem cells which have bit reported before.

qiaoli@umich.edu

Notes: