

IL-10 blockade increases the therapeutic efficacy of effector B cells in cancer adoptive immunotherapy by modulating host cellular and humoral antitumor immunity

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The role played by B cells in the host immune response to cancer is complex and controversial. We have reported the antitumor reactivity of adoptively transferred effector B cells in several tumor models. To understand the mechanisms by which B cells mediate tumor regression, we used the spontaneous metastasis 4T1 breast cancer model and IL-10^{-/-} syngeneic Balb/c mice to generate IL-10^{-/-} tumor-draining lymph nodes (TDLN). Adoptively transferred IL-10^{-/-} TDLN B cells mediated significantly more effective antitumor immunity than equal numbers of WT TDLN B cells ($p < 0.05$). Activated IL-10^{-/-} effector 4T1 TDLN B cells were capable of killing 4T1 tumor cells directly in a tumor antigen specific manner in *in vitro* cytotoxicity assays independent of antibody and complement. Adoptive transfer of IL-10^{-/-} TDLN B cells resulted in the induction of host cellular and humoral antitumor immunity significantly more than adoptive transfer of WT TDLN B cells ($p < 0.05$). This was evident by significantly shifted cytokine production (e.g. up-regulated IFN-gamma and IL-2 production by host T cells, but down-regulated IL-10 production by host B cells). In addition, adoptively transferred IL-10^{-/-} TDLN B cells increased the production of tumor-reactive IgG which bound to 4T1 tumor cells. Furthermore, IL-10^{-/-} TDLN B cell infusion significantly increased tumor cell lysis (CTL) activity mediated by host B cells as well as T cells in an immunologically specific fashion. Our results indicate that depletion of IL-10-producing B cell subsets may represent an effective strategy to augment the therapeutic efficacy of TDLN B cells used in adoptive immunotherapy.

Biography

Qiao Li, Ph.D., a Research Assistant Professor in the Department of Surgery at the University of Michigan has had his research focused on tumor immunology and cancer immunotherapy. His work both in preclinical studies and in clinical trials has involved the treatment of different tumors, including patients with advanced melanoma and renal cancers. These treatment approaches utilize various immune strategies, such as T cells, B cells, and dendritic cells as well as targeting of cancer stem cells.

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