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Cancer stem cell vaccine significantly reduced local tumor relapse and prolonged animal survival in the adjuvant setting

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Therapeutic efficacy of cancer is limited by both local and distant recurrence. Effectively preventing local tumor recurrence remains a significant challenge. The existence of micro metastasis at the time of tumor resection represents an even greater therapeutic challenge, since 90% of tumor deaths are due to tumor metastasis. There is increasing evidence that many cancers are driven and maintained by cancer stem cells (CSCs) which contribute to tumor recurrence and metastasis. Targeting CSCs may thus increase the therapeutic efficacy of current cancer treatment. We described a strategy to target CSCs using CSC-dendritic cell (DC) vaccination. However, the efficacy of CSC targeted therapeutics may be greatest when they are deployed in the adjuvant setting. In this study, two mouse models were utilized: established s.c. SCC7 tumors were surgically removed from mice followed by treatment using $ALDH^{high}$ SCC7 CSC-DC vaccine, which significantly reduced local tumor relapse and prolonged animal survival. This effect was significantly augmented by simultaneous administration of anti-PD-L1 mAb. In the minimal disease setting of D5 melanoma, $ALDH^{high}$ CSC-DC vaccination significantly inhibited tumor growth, reduced spontaneous lung metastases resulting in increased survival. CCR10 and its ligands were down-regulated on ALDHhigh D5 CSCs and in lung tissues respectively in animals subjected to ALDHhigh D5 CSC-DC vaccination. Down-regulation of CCR10 by siRNA significantly blocked tumor cell migration *in vitro* and metastasis *in vivo*. T cells harvested from $ALDH^{high}$ D5 CSC-DC vaccinated animals selectively killed the $ALDH^{high}$ D5 CSCs. As a result, CSC-DC vaccination significantly decreased the percentage of $ALDH^{high}$ cells in residual tumors. These data indicate that, when used in an adjuvant setting, ALDHhigh CSC-DC vaccines effectively inhibit local tumor recurrence, reduce spontaneous lung metastasis and prolong animal survival; compared with traditional DC vaccines and that simultaneous PD-L1 blockade can significantly enhance this effect.

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.

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