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Anti-CTLA-4 Antibody scFv Producing Recombinant *Bifidobacterium* Secretes CTLA-4 Blocker Specifically Inside Hypoxic Tumor and Suppresses Tumor Growth in Syngeneic Mice Model

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Anti-PD-1 antibody and anti-CTLA-4 antibody showed notable efficacy and the combination complimentarily enhanced antitumor benefit. Nevertheless, either single-agent therapy or combination therapy is facing immune-related adverse events (irAEs), which are major cause of treatment discontinuation. Non-specific systemic activation of normal immune system by the therapy is one of major reasons to cause the problems. Approaches to increase the delivery of checkpoint blockers to tumor site may minimize the irAEs and improve the response rate in patients.

In an aim to improve efficiency of anti-cancer drug delivery, we have been developing *in situ* Delivery and Production System (*i*-DPS) by modifying a non-pathogenic anaerobic bacterium, *Bifidobacterium*, which localizes and proliferates only in the hypoxic environment like solid tumors after I.V. administration and also produces anticancer proteins, enzymes or other pharmacologically active molecules selectively at the tumor site. Here we present anti-CTLA-4 antibody scFv producing *i*-DPS in cancer immunotherapy, which could be specifically delivered to and amplified only at the hypoxic sites of solid tumors.