Dendritic Cell-based Immunotherapy Against Hepatocellular Carcinoma (HCC)

Department of Biological Science, Sungkyunkwan University

Yong-Soo Bae

Dendritic cell (DC)-based immunotherapy has been expected to shed lights on the field of cancer treatments. However, even in the murine model, DC-based immunotherapy has not been as much effective as expected in most solid tumor. Our investigation was initiated to identify what causes the limitations of DC-based immunotherapy in solid tumor. We found that the limitation of DC vaccine to solid tumor is likely due to the tumor-mediated TGF-β rather than insufficient immune induction. In fact, the CTL response induced by DC vaccine was quite sufficient and functional for the inhibition of tumor recurrence metastasis after surgery. These results suggest the potential of DC immunotherapy in tumor patients for blocking disease progression by inhibition of tumor metastasis and/or tumor recurrence after surgery or any other primary treatment.

As a therapeutic option for primary tumors in hepatocellular carcinoma (HCC) patients, surgical and/or local ablative treatments have been currently undergone. However, local recurrence or metastases frequently occur after these treatments, and there is no other option available for further treatments of recurrent or metastatic HCC. Recently, several studies have suggested that induction of antitumor immunity is advisable to treat the patients with HCC. In this study, we investigated the efficacy of DC vaccine, which is enforced with topical imiquimod, TLR-7 agonist, to treat patients with HCC. We developed murine HCC model using recombinant MH134 cells stably expressing human HCC specific and associated antigens, which are expressed at a high frequency in Korean HCC patients. Tumor-bearing mice were treated with DC vaccines pulsed with recombinant antigens as a form of fusion protein linked with CTP (cytoplasmic transduction peptide) to induce a strong CTL. The efficacy of DC vaccine was evaluated in the aspects of tumor response, overall survival, inhibition of metastasis, and antitumor immune responses. In the present experiments, DC vaccine was found to be very effective to induce antigen-specific immune response which was functional to

control HCC in both preventive and therapeutic models of HCC. Furthermore, topical application of TLR-7 agonist improved the antitumor effects of DC vaccine.

Based on these pre-clinical studies, we performed phase I/IIa clinical studies to evaluate the feasibility, safety and efficacy of CTP-attached Ag-pulsed DC vaccine in patients with HCC. Twelve patients were enrolled for this clinical study. DC vaccine was well tolerated during the treatment without any severe adversary effects. Clinical outcome was strongly associated with antitumor immunity induced after DC vaccination. Clinical data will be presented and discussed in my talk. Our results imply that Ag-pulsed DC vaccine particularly enforced with topical TLR-7 agonist has a potential to give a promising clinical benefit to patients with HCC when treated after well established primary treatments.