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Moderate anti-tumor effect of the nanoliposomal anti-PCSK9 vaccine in BALB/c mice bearing colorectal cancer.

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Topic(s): Cardio-Oncology

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Background: The higher levels of low-density lipoproteins (LDL) cholesterol (LDL-C) have been reported to correlate with higher prevalence and risk of colon cancer. Proprotein convertase subtilisin/kexin 9 (PCSK9) function, through reducing protein levels of liver LDL receptor, leads to elevated levels of plasma LDL-C.

Purpose: Here, we evaluated anti-tumor effect of nanoliposomal anti-PCSK9 vaccine in mice bearing colon carcinoma.

Methods: To formulate nanoliposomal anti-PCSK9 vaccine, liposome nanoparticles prepared by lipid-film hydration method were covalently attached to immunogenic PCSK9 peptide. The liposomal vaccine formulation was adsorbed to Alum adjuvant (L-IFPTA+) and injected subcutaneously four times with a bi-weekly interval in BALB/c mice. Two weeks after the last immunization, the vaccinated and unvaccinated mice were subcutaneously inoculated with CT26 colon cancer cells into the right flank. After tumor mass was palpable (approximately 10 mm3), the mice were randomly divided into three groups and involved to different treatments: (1) PBS (untreated control), (2) vaccine group, and (3) Doxil®(positive control) group which involved unvaccinated tumor-bearing mice who received Doxil®. To study therapeutic efficacy, mouse body weight, tumor size, and survival were monitored in a 3-day interval for 50 days.

Results: The nanoliposomal anti-PCSK9 vaccine could efficiently induce specific antibodies against PCSK9 in BALB/c mice, and thereby reduce plasma level and function of PCSK9. Tumor size in the vaccinated mice was significantly lower than in Doxil and the control mice. Tumor size analysis revealed that time to reach endpoint (TTE) of the vaccine group was slightly but not significantly higher than that of Doxil and the control groups. The vaccinated mice survived slightly but not significantly longer than Doxil and the control mice. The vaccinated mice’s life was prolonged by 24.4 % as compared with the control mice, while it was increased by 9.8% in Doxil group (see Figure below).

Conclusions: Our findings declare that the nanoliposomal anti-PCSK9 vaccine not only have no harmful effects, but also can mildly reduce tumor growth, and enhance live span and survival in mice bearing colon cancer.
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Figure. Anti-PCSK9 vaccine efficacy. (A) L-IFPTA+ vaccine could induce anti-PCSK9 antibody titers (ODmax2) upon 4 immunizations in a bi-weekly interval. (B) Concentrations of plasma PCSK9 in the vaccine and control group. (C) Direct detection of antibodies bound to plasma PCSK9 in the plasma samples from vaccinated and control mice. (D) In vitro PCSK9/LDLR binding assay.