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May, 2023

NOF EXHIBITS AND PRESENTS A POSTER AT ASGCT 26TH ANNUAL MEETING (May 16- 19)

NOF CORPORATION is exhibiting and presenting a poster at ASGCT 26th Annual Meeting: American Society of Gene & Cell Therapy, held at Los Angeles Convention Center from May 16 to 20 (Booth#525).

Conference website:
https://annualmeeting.asgct.org/

Poster Presentation Title:
Self-Adjuvating Lipid Nanoparticle mRNA Vaccine Elicits T-Cell Responses and Protects Against Immune Challenge

Date and Time:
May 18, 2023 12:00pm-1:30pm

Poster Board Number
1168

Abstract:

Nucleic acid vaccines, DNA and messenger RNA (mRNA), have emerged as promising modalities for infectious disease and for cancer immunotherapy due, in part, to shortened manufacturing cycles and high potency. Currently, there is limited understanding of the mechanisms of antigen presentation and induction of specific T-Cell responses critical to long-term immunity. Lipid nanoparticles (LNP) composed of ionizable lipids are important components of such vaccines as they can convey and present the nucleic acid effectively to the immune system. Further improvements in LNP carriers require a reduction in the 1) systemic toxicity, 2) improved endosomal escape, 3) potent and T-cell specific adjuvating function and 4) targeting to specific antigen presenting cells.

Previously we have reported that lipid nanoparticles composed of a novel ionizable, biodegradable lipid ("SS-Lipid") can deliver pDNA or mRNA in mice to liver, solid tumors, and other organs via the IV route and achieve high levels of expression. We also evaluated the safety of the lipids in mice where total lipid doses of up to 175 mg/kg were well tolerated.

We next evaluated the delivery of DNA and RNA vaccines via the SC route. Multiple SS-Lipid derivatives were synthesized and identified one lipid (SS-EC) that specifically activated macrophage cell in vitro. Antibody generation response was assessed in BALB/c mice with SS-EC 1.5x μg OVA mRNA injected 3X at weekly intervals and compared with immunization with OVA protein+polyI:C. SS-EC LNP produced a 2.2X higher titer compared with OVA-polyI:C control. To assess induction of Cytotoxic T-Cell activity, SS-EC-LNP

carrying OVA-encoding mRNA or Luciferase-encoding mRNA were administered at a dose of 0.05 μg of mRNA. The CTL percent lysis activity at 1 week was 75% (SS-EC_OVA-mRNA) of pulsed antigen cells. Sufficient CTL activity was not obtained with other DOTAP liposome, SS-EC_Luc-mRNA and empty LNP. We then evaluated if robust CTL responses could demonstrate activity against solid tumors. Mice were injected with OVA expressing E.G7 cells as a model for disseminated malignant disease, and treated with SS-EC LNP OVA-mRNA (0.2 μg) after 10 days or SS-EC Luc mRNA as negative control. Tumor growth was significantly repressed in the test animals with negligible growth by day 25. Additional data on the development of a room temperature stable formulation of SS-Lipid mRNA drug product will be presented.

We here demonstrate that a novel ionizable lipid SS-EC specifically activates macrophages in vivo and this response is correlated with antibody expression and Cytotoxic T-Cell activity. T-Cell responses were shown to be effective in limiting growth of tumor cells in a disseminated disease model. Further efforts are needed to optimize the dosage and formulation towards achieving a single dose vaccine product. These findings suggest LNP composed of SS-EC can be effective delivery systems for DNA and RNA vaccines.

Visit our booth #525 during the conference, or contact our regional offices below:

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