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April, 2022

NOF EXHIBITS AND PRESENTS A POSTER AT ASGCT 25th Annual Meeting (May 16-18)

NOF CORPORATION is exhibiting and presenting a poster at ASGCT 25th Annual Meeting: American Society of Gene & Cell Therapy, held at Walter E. Washington Convention Center, Washington, D.C. between May 16th and May 18th (Booth# 221).

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

Poster Presentation Title:
Ionizable Lipid Nanoparticle Platform for mRNA Therapeutics with Room Temperature Stability

Date and Time:
May 17, 2022 at 17:30-18:30

Abstract:
The recent FDA approval of COVID-19 vaccines composed of mRNA loaded ionizable lipid nanoparticles (mRNA-LNP) has increased interest in novel application of this modality including cancer immunotherapy. However, mRNA applications have been limited by immunogenicity, poor drug product stability and low in vivo expression. Here we report on our efforts to develop COATSOME® SS-Lipid: an mRNA-LNP composed of biodegradable ionizable lipids with improved safety profile, increased gene expression and room temperature stable lyophilized drug product.
Previously we demonstrated that SS-lipids can be engineered to degrade in response to specific intracellular signals yet provide extended stability in circulation. Biodegradable lipids also demonstrate excellent safety profile in rodents with limited immunogenicity at total lipid doses as high as 160 mg/kg. For the vaccine application, we identified two new SS-Lipids “SS-EC” and “SS-E” with high macrophage activation in an *in vitro* interferon-β production assay. We next assessed antibody response in mice immunized with OVA mRNA-LNP vs conventional immunization with OVA protein and Poly I:C adjuvant. Although IgG induction required multiple doses and sufficient titer was seen only after 20 days, anti-OVA IgG titers were approximately 2X higher in the LNP group vs the OVA protein immunized group. These results suggest that for mRNA LNP T-Cell immunity emerges first and B-cell immunity is delayed for several weeks, possible due to inefficient antigen presentation. Examination of draining lymph nodes showed SC injected LNP appeared within 24 hours, and flow cytometry analysis of the cells that had taken up the LNPs showed that the SS-E LNPs were largely taken up by macrophages and a small number of dendritic cells. We found that the transient deletion of CD169+ macrophages, unexpectedly enhanced the activity of the vaccine. Finally, we evaluated the interim stability of

a lyophilized drug product of the SS-Lipid hEPO mRNA LNP stored under different temperatures at the 12 week timepoint. The mRNA expression activity *in vivo* of the lyophilized samples was comparable to that of the fresh LNP across all storage conditions.
Conclusion: We showed evidence of robust T-cell responses with a single shot mRNA-LNP vaccine, consistent with presentation of exogenous mRNA antigens in the MHC-I complex. Our mRNA-LNP was able to induce antibody responses exceeding that of a conventional OVA subunit vaccine. Furthermore, we have developed a lyophilized drug product with room temperature stability that overcomes many of the cold-chain handling limitations of currently approved mRNA vaccines.

Visit our booth #221 during the conference, or contact our regional offices below:

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