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703.CELLULAR IMMUNOTHERAPIES: BASIC AND TRANSLATIONAL

Lipid Nanoparticle Library Towards Development of Next Generation Genomic Medicines

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Ionizable amino lipids are a major constituent of the lipid nanoparticles for delivering nucleic acid therapeutics (e.g., DLin-MC3-DMA in ONPATTRO®, ALC-0315 in Comirnaty®, SM-102 in Spikevax®). Scarcity of lipids that are suitable for cell therapy, vaccination, and gene therapies continue to be a problem in advancing many potential diagnostic/therapeutic/vaccine candidates to the clinic.

Herein, we describe the development of novel ionizable lipids to be used as functional excipients for designing vehicles for nucleic acid therapeutics/vaccines in vivo or ex vivo use in cell therapy applications. We first studied the transfection efficiency (TE) of LNP-based mRNA formulations of these ionizable lipid candidates in primary human T cells and established a workflow for engineering of primary immune T cells. We then adapted this workflow towards bioengineering of CAR constructs to T cells towards non-viral CAR T therapy. Lipids were also tested in rodents for vaccine applications using self-amplifying RNA (saRNA) encoding various antigens. We have then evaluated various ionizable lipid candidates and their biodistribution along with the mRNA/DNA translation exploration using various LNP compositions. Further, using ionizable lipids from the library, we have shown gene editing of various targets in rodents.

We believe that these studies will pave the path to the advancement in nucleic acid based therapeutics and vaccines, or cell & gene therapy agents for early diagnosis and detection of cancer, and for targeted genomic medicines towards cancer treatment and diagnosis.

Disclosures Jain: *Precision NanoSystems:* Current Employment. **Nazaripour:** *Precision NanoSystems:* Current Employment. **Chen:** *Precision NanoSystems:* Current Employment. **Abraham:** *Precision NanoSystems:* Current Employment. **Yee:** *Precision NanoSystems:* Current Employment. **Sadat:** *Precision NanoSystems:* Current Employment. **Mehar Namala:** *Precision NanoSystems:* Current Employment. **Son:** *Precision NanoSystems:* Current Employment. **Chemmannur:** *Precision NanoSystems:* Current Employment. **Tickner:** *Precision NanoSystems:* Current Employment. **Anantha:** *Precision NanoSystems:* Current Employment. **Sharma:** *Precision NanoSystems:* Current Employment. **Abbina:** *Precision NanoSystems:* Current Employment. **Thambatti:** *Precision NanoSystems:* Current Employment. **Mayya:** *Precision NanoSystems:* Current Employment. **Soon:** *Precision NanoSystems:* Current Employment. **Paquette:** *Precision NanoSystems:* Current Employment. **Thomas:** *Precision NanoSystems:* Current Employment. **Nguyen:** *Precision NanoSystems:* Current Employment.