A Novel Ionizable Lipid JK-102 Enables Efficient mRNA Delivery and Robust T-Cell Responses Comparable to SM-102

Shengyong Yan, Jiadong Fan, Biao Liu, Ke Xia, Qingbin Wang*, Xuan Zhao, Lihong Guo, JenKem Technology Co., Ltd.
Corresponding author: * qingbinwang@jenkem.com

JenKem Technology

Lipid nanoparticles (LNPs) are a leading platform for mRNA delivery, with ionizable lipids critically influencing their efficacy and immunogenicity. In this study we evaluated a novel ionizable lipid, JK-102, in comparison with the clinically validated lipid SM-102.
LNPs encapsulating luciferase, GFP, or ovalbumin (OVA) mRNA were formulated separately with JK-102, and SM-102. In vitro studies in murine (DC2.4, RAW264.7) and human (A549, 293T) cell lines showed comparable luciferase expression between JK-102 and SM-102 containing LNPs. Following intramuscular (IM) administration in mice, the JK-102 LNP demonstrated comparable or enhanced in vivo luciferase expression, compared to the SM-102 LNP. Ex vivo imaging revealed both JK-102 LNP and SM-102 LNP distributed in the liver, draining lymph nodes, and spleen. GFP expression was detected in splenic immune cells, including dendritic cells and B cells. Immunization with OVA mRNA-LNPs induced robust antigen-specific T-cell responses, as measured by IFN-γ ELISpot, with the JK-102 LNP showing comparable immunogenicity to SM-102 LNP.

In conclusion, JK-102 LNPs support efficient mRNA expression, comparable biodistribution to SM-102, and strong cellular immune responses, highlighting their potential as an alternative platform for mRNA vaccine delivery.

JK-102 LNP demonstrates luciferase expression comparable to SM-102 LNP across murine and human cell lines

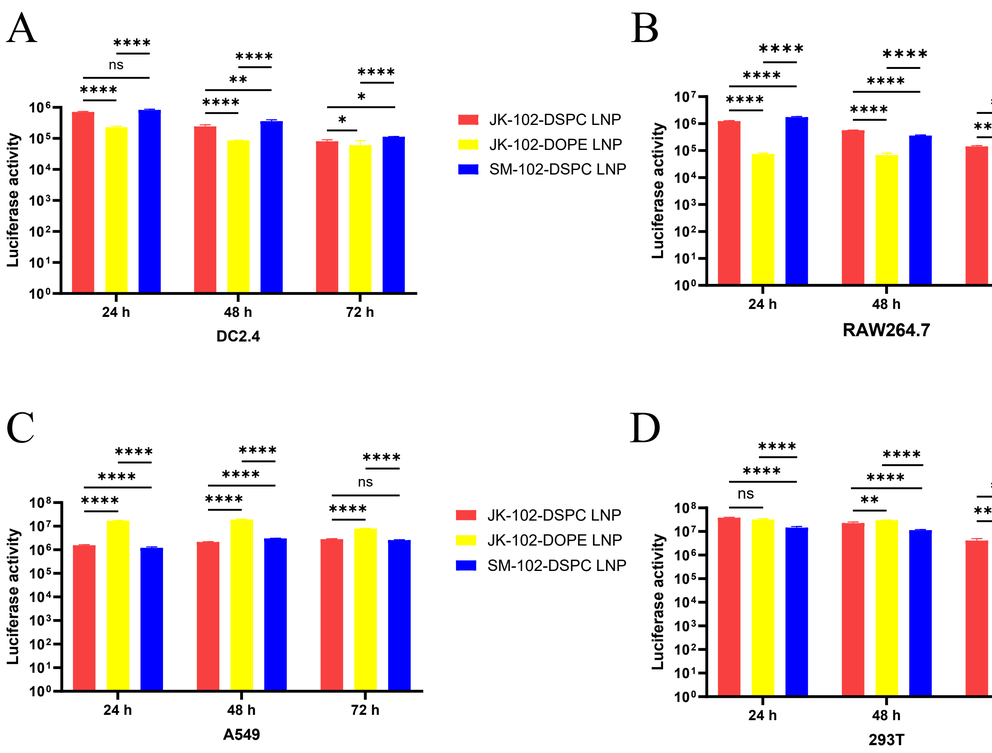

Figure 1. Luciferase mRNA expression in cells transfected with LNP formulations. Luciferase mRNA was encapsulated in lipid nanoparticles (LNPs) composed of the ionizable lipid JK-102, helper lipid 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) or 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), cholesterol, and DMG-PEG2000. Luminescence was measured at 24, 48, and 72 h post-transfection in murine immune cell lines DC2.4 (A) and RAW264.7 (B), and human cell lines A549 (C) and 293T (D). Statistical significance was determined by two-way ANOVA. ns, $p > 0.05$; ****, $p < 0.0001$.

Enhanced in vivo luciferase expression with JK-102 LNP compared with SM-102 LNP

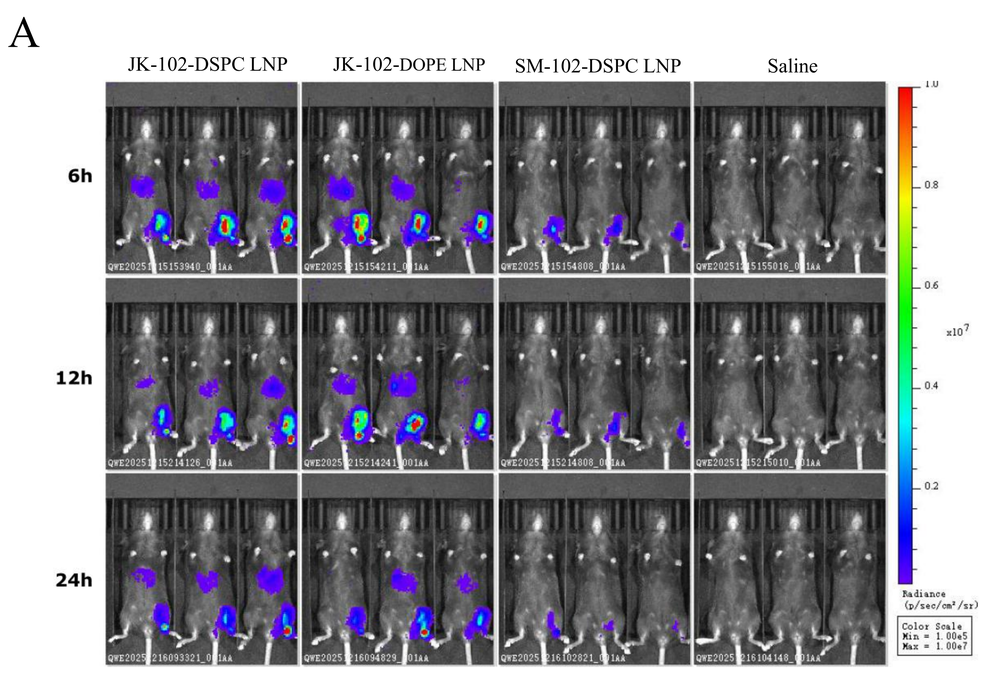

Figure 2. In vivo biodistribution and expression of luciferase mRNA-LNPs. (A) C57BL/6 mice (n = 3) were intramuscularly (IM) injected with 5 μg of luciferase mRNA-LNPs. Bioluminescence imaging was performed at 6, 12, and 24 h post-injection using an IVIS system. (B) Total photon flux was quantified at indicated time points. Statistical significance was determined by two-way ANOVA. ns, $p > 0.05$; *, $p < 0.05$.

Ex vivo biodistribution of JK-102 LNP reveals accumulation in liver, draining lymph nodes, and spleen

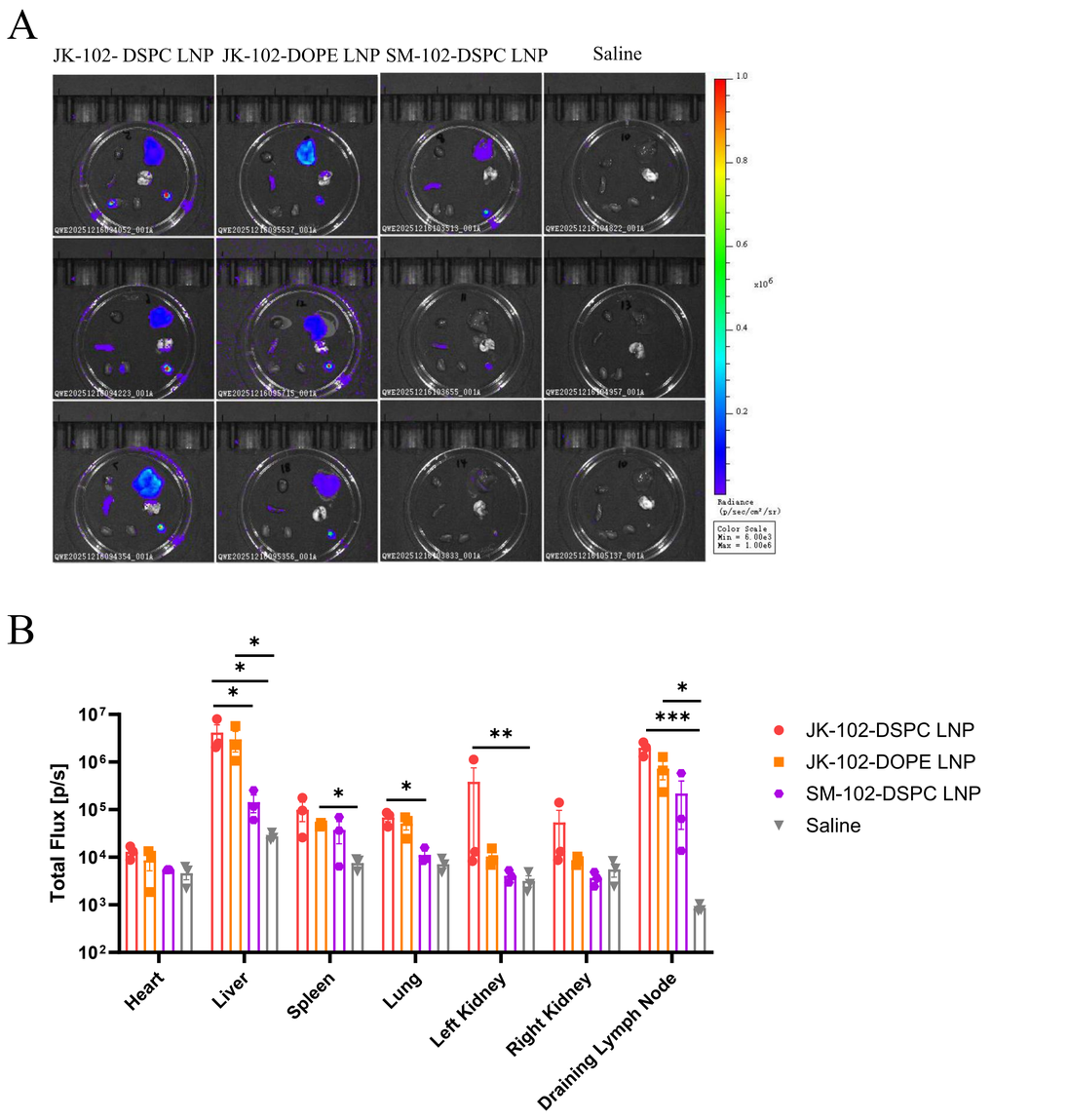

Figure 3. Ex vivo organ distribution of luciferase mRNA-LNPs. (A) C57BL/6 mice (n = 3) were IM injected with 5 μg of luciferase mRNA-LNPs. At 24 h post-injection, mice were sacrificed and organs were harvested for bioluminescence imaging. (B) Total photon flux in collected organs was quantified. Statistical significance was determined by two-way ANOVA. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

JK-102 LNP mediates GFP expression in splenic B cells and dendritic cells

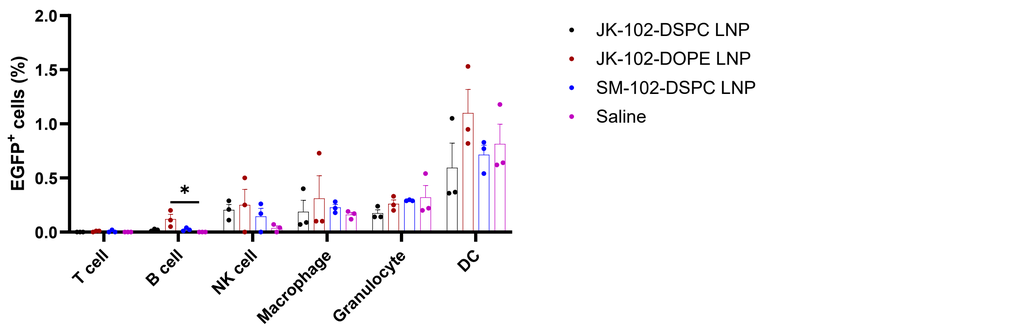

Figure 4. Cell-type distribution of GFP expression in the spleen. C57BL/6 mice (n = 3) were IM injected with GFP mRNA-LNPs. Spleens were collected 24 h post-immunization, and GFP expression was analyzed across immune cell subsets.

JK-102-OVA induces robust antigen-specific T-cell responses comparable to SM-102-OVA

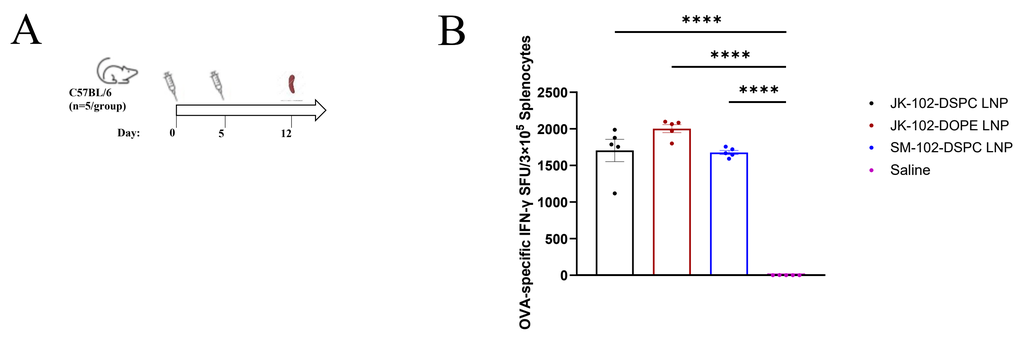

Figure 5. Evaluation of antigen-specific T-cell responses by ELISpot. (A) Immunization and sampling scheme. (B) C57BL/6 mice (n = 5) were IM immunized on Day 0 (prime) and Day 5 (boost) with 15 μg of OVA mRNA-LNPs. Spleens were collected on Day 12, and antigen-specific T-cell responses were assessed by IFN-γ ELISpot.