

Manuscript #	NCOMMS-19-01080
Current Revision #	0
Other Versions	NCOMMS-19-01080A NCOMMS-19-01080B NCOMMS-19-01080C NCOMMS-19-01080D
Submission Date	13th January 19
Current Stage	Resubmission received
Title	Nucleoside-Modified VEGFC mRNA Induces Organ-Specific Lymphatic Growth and Reverses Experimental Lymphedema
Manuscript Type	Article
Manuscript Comment	SUGGESTED REVIEWERS ===== Dr. Gou Young Koh (gykoh@kaist.ac.kr): an expert on studying the in vivo functions of lymphatics (Korea Advanced Institute of Science and Technology, South Korea) Dr. Tsutomu Kume (t-kume@northwestern.edu): an expert on lymphatic vascular development (Northwestern University School of Medicine, USA) Dr. Ugur Sahin (sahin@uni-mainz.de): expert on mRNA therapeutics (Johannes Gutenberg University, Germany) REVIEWERS TO EXCLUDE ===== Dr. Kari Alitalo (University of Helsinki, Finland) Dr. Stanley G. Rockson (Stanford University School of Medicine, USA) Dr. Giuseppe Ciaramella (Beam Therapeutics, USA) We would like to exclude them as reviewers due to conflicting scientific interests.
Corresponding Author	Dr Zoltan Jakus (jakus.zoltan@med.semmelweis-univ.hu) (Semmelweis University)
Contributing Authors	Dr Dániel Szóke , Laszlo Balint , Dr Gábor Kovács , Kitti Ajtay , Petra Aradi , Andrea Styevkone Dinnyes , Barbara Mui , Ying Tam , Thomas Madden , Professor Katalin Karikó , Raghu Kataru , Dr Michael Hope , Babak Mehrara , Professor Drew Weissman , Dr Norbert Pardi
Authorship	Yes
Abstract	Lack or dysfunction of the lymphatics leads to secondary lymphedema development that seriously reduces the function of the affected organs and results in degradation of quality of life. Currently, there is no definitive treatment option for lymphedema. Here, we utilized nucleoside-modified mRNA encapsulated in lipid nanoparticles (LNPs) encoding murine Vascular Endothelial Growth Factor C (VEGFC) to stimulate lymphatic growth and function and reduce lymphedema in mouse models. We demonstrated that administration of a single low dose of VEGFC mRNA-LNPs induced durable, organ-specific lymphatic growth and active lymphatic function in newly formed vessels. Importantly, VEGFC mRNA-LNP treatment reversed experimental lymphedema without inducing any obvious adverse events. Collectively, we present a novel application of the nucleoside-modified mRNA-LNP platform, describe a model for identifying the organ-specific physiological and pathophysiological roles of the lymphatic system, and propose an efficient and safe treatment option that may serve as a novel therapeutic tool to reduce lymphedema.
Subject Terms	Biological sciences/Biotechnology/Nucleic-acid therapeutics Biological sciences/Developmental biology/Lymphangiogenesis Health sciences/Medical research/Preclinical research
Show Author Information	Allow Reviewers to see Author information.
Competing interests policy	Yes there is potential Competing Interest. In accordance with the University of Pennsylvania policies and procedures and our ethical obligations as researchers, we report that Katalin Karikó and Drew Weissman are named on patents that describe the use of nucleoside-modified mRNA as a platform to deliver therapeutic proteins. Drew Weissman and Norbert Pardi are also named on a patent describing the use of modified mRNA in lipid nanoparticles. We have disclosed those interests fully to the University of Pennsylvania, and we have in place an approved plan for managing any potential conflicts arising from licensing of our patents. No competing interests from other authors have been reported.

Applicable Funding Source	No Applicable Funding
----------------------------------	-----------------------

Manuscript Items

1. Author Cover Letter [PDF \(138KB\)](#)
2. Article File [PDF \(24360KB\)](#)
3. Szoke et al VEGFC mRNA-LNP Supplementary figures 12-31-2018 v3.pdf [PDF \(4146KB\)](#)
4. Reviewer Zip File "Zip of files for Reviewer"
5. Reporting Summary [PDF \(84KB\)](#)

More Manuscript Info and Tools

[Send Manuscript Correspondence](#)

[Decision Summary](#)

[Check Status](#)



[tracking system home](#) | [privacy policy](#) | [cookie policy](#) | [manage cookies](#)