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January 24, 2020

Ronald Myers, PhD
Senior Science Editor
The Journal of Visualized Experiments
E-mail: ronald.myers@jove.com

Dear Dr. Myers,

We submit a revised original research manuscript entitled "Delivery of Modified mRNA in a Myocardial Infarction Mouse Model" for consideration for publication in The Journal of Visualized Experiments (*Jove*). The data are unpublished and are not under consideration by any other journal. All authors have approved the manuscript for submission.

Myocardial infarction (MI) remains a major cause of morbidity and mortality and is associated with significant societal and economic burden. In order to develop better therapeutics and improve outcomes for patients, researchers are focusing to evaluate the role of gene therapy in the mitigating the heart disease.

Till date, various traditional genes delivery methods have been employed in the clinics in attempt to increase the expression of a specific protein in the heart. Despite the initial success with these integrating vectors, their use in therapeutic medicine has declined due to complications like poor and uncontrolled expression of the delivered genes. In contrast, modified RNA (modRNA) offers gene transfer both dividing and non-dividing mammalian cells that mediate fast, robust, transient expression of proteins in the targeted cells or tissue and thus has become a promising avenue in ischemic heart disease research.

Thus, in this protocol we present a standardized and optimized method of preparation and delivery of modRNA intracardiac injection in mouse MI model to maximize modRNA delivery efficiency. With this paper, we attempt to make modRNA-based cardiac delivery accessible and consistent for *in vivo* applications.

The initial reviews were positive but pointed out few shortcomings in the manuscript. In the revision, we have comprehensively addressed all these issues that substantially strengthen the manuscript.



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We hope you will find our study acceptable for review and publication in *Jove*.

Please do not hesitate to contact me with any questions you might have.

Lior Zangi, PhD

A handwritten signature in blue ink that reads "Lior Zangi". The signature is written in a cursive, flowing style.

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