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To: *Journal of Visualized Experiments (JoVE)*

From: Negin P. Martin, Ph.D.

Subject: Manuscript Submission

April 20<sup>th</sup>, 2018

Dear editorial board,

Please find attached our manuscript entitled " Laser-assisted Lentiviral Gene Delivery to Mouse Fertilized Eggs" for consideration to publish in *JoVE*. We were very excited to be invited by Dr. Indrani Mukherjee to submit a manuscript.

In this manuscript, we validate an effective and original method for delivering genes to mouse fertilized eggs by combining laser-perforation of zona pellucida and lentiviral gene delivery. Multiple departments at our Institute combined experiences to develop this method for gene delivery to mouse fertilized eggs. This method has been received very well by mouse geneticist as an alternate method for spatiotemporal genetic manipulation of mouse embryos. In this protocol, instead of delivering genes to mouse fertilized eggs one at a time utilizing pronuclear microinjection, the gene(s) of interest are delivered rapidly and in bulk without micromanipulation. We demonstrate that XYClone laser perforation of zona which is typically used for *in vitro* fertilization, also provides a venue for lentiviruses to diffuse across the zona and to infect mouse embryos. We provide a detailed protocol for successful gene delivery in our manuscript. Once the zona barrier is permeablized by the XYClone laser, it makes embryos accessible for gene delivery via various types of viruses. Thus, providing a powerful tool for delivering genes to control early stage cell fate, to influence the differentiation of embryonic stem cells, and to create transgenic, knockdown or knockout animal models. We believe that our findings will generate broad interest in your readership and hope that our paper merits publication in *JoVE*.

We will be happy with selection of any member of the *JoVE* editorial board for review. I would like to thank you in advance for considering our manuscript. Should you have any questions or concerns please feel free to contact me.

Sincerely yours,

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