Calibr
at Scripps Research

11119 North Torrey Pines Road
La Jolla, CA 92037

Dear Editor,

Enclosed is a revised version of the manuscript entitled, "Using In Vitro and In-cell SHAPE to Investigate Small Molecule induced pre-mRNA Structural Change" by Wang et al. We appreciate the thoughtful editorial comments of the journal, and based upon the feedback, we have improved and revised the manuscript text, the figures and the figure legends.

A direct thank you to Dr. Cao also for the time spent by phone and emails to help us make the decisions to focus upon the key aspects of the methodology. We agree to focus the filming upon the *in vitro* SHAPE and have make the changes in the highlighting of the manuscript accordingly. Specific responses to each comment are detailed below.

Editorial comments:

Changes to be made by the Author(s) regarding the written manuscript:

Please note that your protocol will be used to generate the script for the video and must contain everything that you would like shown in the video. Please review all the highlighted steps to ensure that they are continuous and tell a complete story of the Protocol. Please include all relevant details that are required to perform the step in the highlighting. For example, the filmed content currently starts with recovering the RNA from the gel slice (step 1.1.13) without introducing how the gel slice is prepared. Similarly, the highlighted step 1.5.2 uses sample prepared in step 1.4.8, which is not highlighted for filming. It does not matter whether preparation of a polyacrylamide gel is a routine technique for a common molecular biology laboratory. It has to be mentioned/filmed if the gel/sample is going to be used in a later highlighted step. Otherwise, the viewers will have no clue where these are coming from when watching the video.

Response: The authors agree with the editor and now the highlighting area has been focused on 1. *In vitro* SHAPE. All highlighting area for in-cell SHAPE has been removed.

Should the unit be W or V? Please check.

Response: We used Watts-constant mode and therefore W is the correct unit.

Best,

Kristen A. Johnson
Principal Investigator
kjohnson@calibr.org
858-242-1009