

To: Meghan A. Berryman
Journal of Visualized Experiments
48 Grove Street, Suite 305
Somerville, MA 02144

19 May 2011

Re: Multiplexed Single Molecule Force Proteolysis Measurements Using Magnetic Tweezers

Dear Meghan Berryman,

We would like to submit our publication, titled "Multiplexed Single Molecule Proteolysis Measurements Using Magnetic Tweezers," for publication in the *Journal of Visualized Experiments*. We realize that initially JOVE had expressed interest in our work on the motor protein myosin VI. However, as explained below, we believe the new single-molecule magnetic tweezers assay we have developed will be even more interesting to JOVE's readership. We've therefore taken the liberty of preparing a manuscript that describes this work, in the hope that you will agree to publish it.

Of the several single-molecule techniques, magnetic tweezers are especially attractive because of their low cost, ease of implementation, and high throughput. Briefly, the most common magnetic tweezers setup consists of two permanent magnets mounted on a simple light microscope. The magnets exert force on micron-sized magnetic beads, which in turn pull on the molecule of interest. Until recently, magnetic tweezers have mostly been used to study DNA biophysics. However, recently we have adapted the canonical magnetic tweezers setup to study the effect of force on the interactions between an enzyme (matrix metalloproteinase 1) and its protein substrate (collagen). Our findings were published in the *Journal of American Chemical Society* (Adhikari et. al. *JACS* 133, 2011), and the manuscript was featured in *Chemical and Engineering News* ("A little tug speeds up collagen cleavage", *C&EN* 89, 2011).

We provide detailed protocols for how to setup and calibrate magnetic tweezers. We also elaborate on our experiments regarding the force-dependent proteolysis of collagen by MMP-1. Our methods will be of exceptional interest to biophysicists who want to study the effect of force on protein unfolding and protein-protein interactions in a cost and time-effective manner. Our methods may help motivate unexpected new avenues of research for molecular biologists, chemical biologists, clinicians, and even developmental biologists who are interested in finding a straightforward way to exert force on their protein of interest. We're excited about this project, and think that JOVE's unique format is exceptionally well suited for sharing it with a wider audience.

Thanks again for approaching my lab about the possibility of publishing our work. We think JOVE is adding a new dimension to the dissemination of scientific research, and would be honored and delighted to see our work in your journal.

Best regards,



Alex Dunn