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Ultra-gentle soft robotic fingers induce minimal transcriptomic response in a fragile marine animal

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The recent invention of ultra-gentle soft robotics opens up the possibility of creating a suite of deep-sea interactive devices that would allow scientists to temporarily immobilize deep-sea organisms, some as delicate as jellyfish, and perform *in-situ* experiments (such as swabbing DNA, imaging morphology, and measuring physiological variables) prior to setting the organism free. However, while the premise of being 'gentle' when handling animals seems intuitive, the hypothesis that newly developed soft robotic grippers have a lower impact on an animal's stress response had remained untested. Herein we present results from a stress-focused experiment that compares the transcriptional response of a jellyfish (*Aurelia aurita*) after various forms of physical manipulation, focusing on the impact of new ultra-gentle soft robotic actuating fingers that were specifically developed for jellyfish but have wider applications (e.g., surgical devices and crop harvesting). We find that soft robotic fingers induce significantly less change in gene expression compared to a more traditional rigid claw-grab.

The aggressiveness of traditional grippers is what recently led engineers collaborating with biologists to develop novel delicate robotic grippers, like the ultra-gentle soft robotic fingers (Video S1 in Supplemental Information, published with this article online) [1], to more tactfully and gently handle animals [2–6]. In the future, these new tools aim to alleviate the need to collect specimens for certain studies, such as population genomics, microbiomics, or continual monitoring of deep-sea organisms. In this study, four experimental treatments were conducted for one minute and consisted of, firstly, a negative control, acclimated without physical manipulation (unstressed); secondly, a positive control, high-stress treatment, held with a rigid claw-grab while shaking; thirdly, a rigid claw-grab, held with a rigid claw-grab with no shaking; and, finally, held with ultra-gentle soft robotic fingers. Each treatment was conducted in triplicate (n = 3 jellyfish). Each jellyfish transcriptome (n = 12) was sequenced with an Illumina NovaSeq 6000 (2 x 100bp). The one-minute time frame is relatively brief (studies often wait ~30 minutes), but was selected to represent a realistic minimum handling

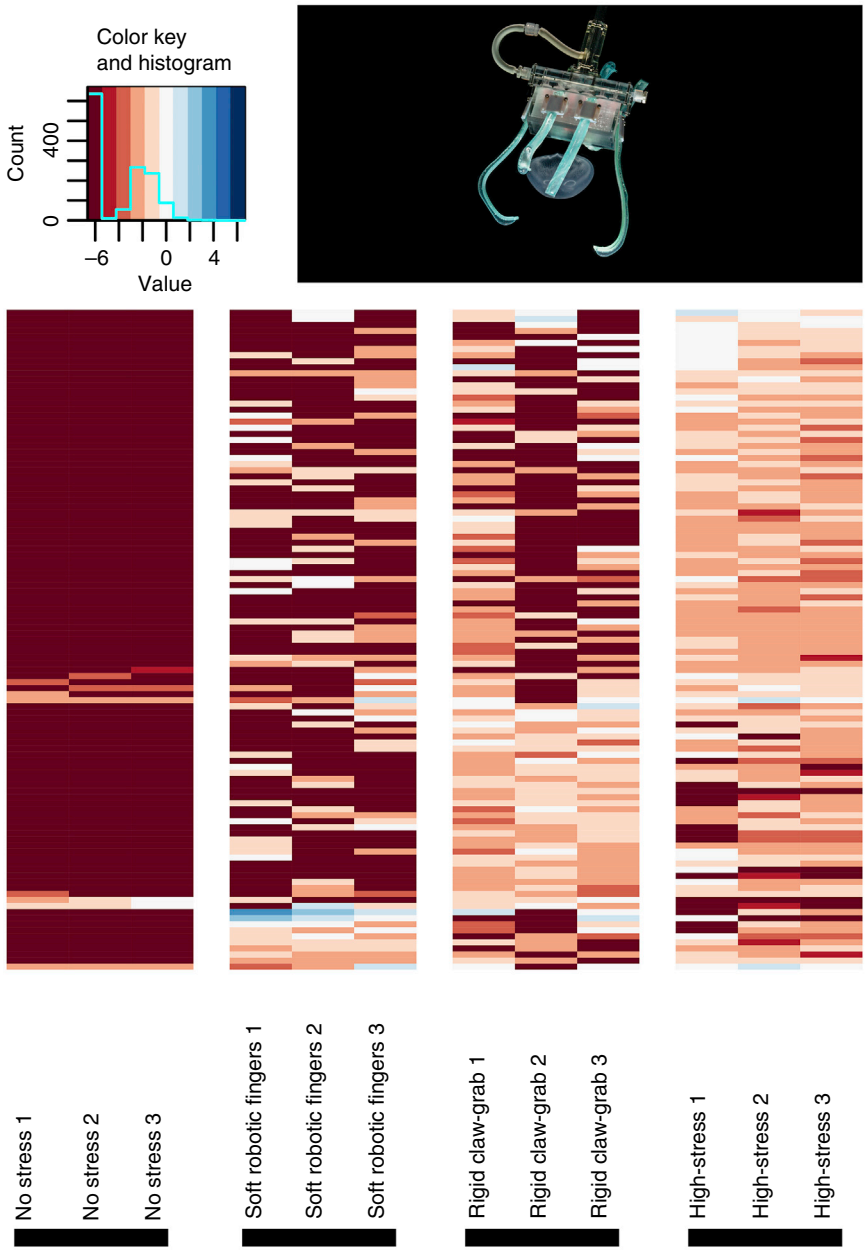

Figure 1. Differential transcription of jellyfish genes across interacting methods.
A heat map showing transcript levels (log_2 transformed counts per million) of all overexpressed transcripts relative to the control (unstressed) across replicate samples for each treatment. Consistent, immediate induction of a larger number of transcripts is observed across replicates of high-stress (positive control) and rigid claw-grab samples in contrast to soft robotic finger replicates. Dark red indicates zero counts for that transcript and sample.

time in the field for transcriptomic sampling or for moving a specimen a short distance (e.g., for experimental ecological work). Additional methods can be found in Supplemental Information.

The differential gene expression results were highly concordant with expectations (Figures 1 and S1). Relative to the unstressed control, the ultra-gentle soft robotic fingers treatment produced the fewest differentially expressed transcripts (11 upregulated; 15 downregulated), the rigid claw-grab had an intermediate number (28 upregulated; 27 downregulated), and the rigid claw-grab with agitation (the positive control) yielded the highest number (92 upregulated; 29 downregulated). Approximately 10% of the differentially expressed transcripts from the soft robotic finger treatment were shared with the high-stress (positive control) treatment, whereas the rigid claw-grab shared over 25% of its differentially expressed transcripts with the high-stress (positive-control) treatment.

Similarly concordant with our predictions, several differentially expressed transcripts appeared to relate to tissue damage or stress response. Q80Y14, a Glutaredoxin-related protein reported to protect cells against apoptosis, was significantly over-expressed in the high-stress (positive-control) treatment relative to the unstressed control, was observed in two out of three replicates in the rigid claw experiment, and was not detected in the unstressed controls or the soft robotic fingers experiment. Q5R6I4, a death domain-containing adapter protein that forms an apoptosis triggering complex, was consistently and significantly over-expressed in the high-stress (positive-control) and rigid claw experiments, but was undetected in unstressed controls and in the soft robotic fingers treatment. Q969X1, an anti-apoptotic protein lifeguard, was consistently and significantly overexpressed in the high-stress (positive-control) experiment relative to the unstressed control, was detected in two of three replicates in the rigid claw experiment, and was present in neither the unstressed controls nor the soft robotic fingers trial. Interestingly, we did not find similar stress markers to previous chemically induced stress experiments using *A. aurita*; however, in addition to a different type of stress, they implemented a far longer experimental treatment time [7].

Our short treatment time led to significant changes in differentially expressed transcripts that mirrored our predictions, but at relatively low levels compared to other studies [8] that often have treatment times of ~30 minutes. Given our significant findings across a relatively short sampling time, it may be possible that *A. aurita* has a reasonably fast transcriptomic response time when dealing with tissue damage, as injury (e.g., amputated appendages) is common in marine invertebrates [9]. Based on the frequency of injury, there is likely selective pressure for rapid self-repair in jellyfish. *Aurelia aurita* can respond to injuries by reorganizing existing parts and rebuilding essential body symmetry often without regenerating lost parts [10].

To our knowledge, this is the first study to quantify the transcriptomic response in a jellyfish in relation to handling methods. This study sets the stage for future research using gentle grippers to examine the physiology of, and interact with, deep-sea lifeforms that are often fragile and long-lived. This type of gripper also reduces mechanical damage to specimens [6] that industrial hard grippers can inflict when handing organisms. Importantly, we have shown that gentle physical handling by a delicate gripper results in a less stressful experience for an animal, as compared to more conventional rigid grippers. This knowledge is especially important for deep-sea biologists in the adoption of soft robotics for *in situ* handling and studying (e.g., swabbing for genetic studies) of organisms that are often fragile, long-lived, difficult-to-access, or endangered. This will help advance deep-sea research in an era where the public is paying particular attention to our collective impact on the environment and its inhabitants, making non-lethal interactions with organisms ever more important. We hope that further inquiries expand on this study by focusing on a diversity of organisms, robotic devices, *in situ* relocations, coupled measurements, and time scales for experimental manipulation of specimens.

SUPPLEMENTAL INFORMATION

Supplemental Information contains one figure, experimental procedures, results, and one video, all of which can be found with this article online at https://doi.org/10.1016/j.cub.2020.01.032.

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