Dear Dr Braiman,

Please find enclosed our manuscript entitled " *Automated behavioural analysis of large C. elegans populations using a wide field of view tracking platform”* that we would like to be considered for publication in Journal of Visualized Experiments.

The nematode worm *C. elegans* is a widely used model organism in biomedical research, as with its simplicity and versatility it is an effective system to study a variety of aspects of a wide range of human diseases. A number of automated platforms have been proposed recently for screening worm phenotypes but have largely focused on monitoring the behaviour of single or limited amounts of worms. Because of these limitations, high throughput multi-parameter platforms, giving access to screening for genes or potential drugs, have remained out of reach.

To address these limitations, we recently developed a Wide Field-of-View Nematode Tracking Platform (WF-NTP) (Perni et al. J. Neurosci. Methods 2018, in press) and successfully applied it to drug and antibody discovery. This platform can be used to study the behaviour of more than 5000 animals in parallel and to report metrics of more than a million worms every week. The unprecedented level of throughput provided by this method allows statistical errors to be very significantly reduced, enabling previously undetectable phenotypic differences to be discovered and opening the concrete possibility of carrying out drug discovery in worms.

The platform has already been successfully used into drug discovery for Alzheimer’s disease (AD) (Habchi et al, 2016,2017) and Parkinson’s disease (PD) (Perni et al., 2017a, 2018 in press). Furthermore the development platform allowed also to set novel protocols to evaluate directly the effects of the administration of antibodies in worms (Aprile et al, 2017, Perni et al., 2017b). Remarkably, one compound identified with this method, squalamine, has being tested in stage 2a clinical trials for PD (Zasloff et al, 2018 in Preparation).

We anticipate that the greatly enhanced ability to detect weak phenotypic differences by using of this platform will have widespread applications in the thousands of laboratories that carry out *C. elegans* research worldwide. The full open source availability of the code and platform, combined with the protocol described in the attached manuscript, will also make it readily accessible to the community.

We suggest the following experts as potential reviewers:

Richard Morimoto, Northwestern University, Chicago, USA.

Franz-Ulrich Hartl, Max Planck Institute of Biochemistry, Munich, Germany.

Judith Frydman, Stanford University, Palo Alto, USA.

Perni M, Casford S and Aprile FAA designed the procedures described in the manuscript, performed the experiments and analyzed the data. Perni M, Casford S and Aprile FAA, Nollen EAA, Knowles TPJ, Vendruscolo M, Dobson CM were involved in the design of the study and wrote the manuscript.

During the preparation and submission of this manuscript, we have been kindly assisted by

Dr Jaydev Upponi.

We very much hope that you will find this manuscript to be of interest to the readers of *JovE* and look forward to hearing from you.

Tuomas Knowles, Michele Vendruscolo and Chris Dobson