*Strasbourg, December 17th 2013*

Dear Editor,

We are submitting a manuscript entitled ´**Ordering cells and embryos in 3 dimensions: a new device for high content screening´**.

Standard cell-based assays are usually performed on flat surfaces, where cells spread and take quasi-2D shapes. In addition, and amongst other limitations, cells are disordered, show heterogeneous phenotypes and some organelles are not properly visualized. This has important consequences, in particular, for screening applications. In contrast, cells *in vivo* are located in a three dimensional environment showing phenotypes and activities very different from those observed on standard ´flat´ assays. This demands new devices and methods to bridge the gap between *in vitro* and *in vivo* conditions with reproducible and standardized conditions.

In this paper, we report the microfabrication and application of a new *in vitro* three dimensional and high-content-screening device for cell-based applications. This method allows the study of cell architecture as well as dynamical processes with high-content-screening characteristics. Our laboratory focuses in the biophysical description of cellular phenomena, such as cytoskeleton organization, cell division and drug screening. Our developed 3D cell culture device and method allow to standardize and to generate order of individual cells in a 3D environment. This device consists of an array of thousands to billions of microcavities, each filled with individual cells, where cell position, shape, and internal cell organization become normalized with a 3D architecture. We report that cells in this configuration showed phenotypes similar to those observed *in vivo*, and most importantly, we identified new dynamic processes that could not be observed using standard assays.

This method is simple, fast and flexible. The device can be easily adapted for different cell types and model systems and can be used for a variety of applications if the procedure is clearly described and characterized. We believe that this new device and method will be useful to the scientific community and this motivated the submission of our work in JoVE's special multimedia format.

This submission is an invited contribution proposed by Rachel Baker and Elizabeth Sheeley. We agreed that, if the manuscript is accepted, we will keep control about the moment it is published because other works currently under preparation should be accepted first. This paper has not been published or is under consideration in another journal. We would like you to consider this manuscript for publication as an article in *JoVE* journal*.*

Sincerely yours,

Daniel Riveline.

**Author contributions:**

D.R. initiated the device and method for fission yeast. V.W. and D.R. designed the approach for mammalian cells. V.W. and D.C. performed the experiments with mammalian cells and *C.* *elegans*. D.R., R.T. and V.W., performed the experiments with yeast. All the authors analyzed the data and wrote the paper. D.R. supervised the project.

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