Microdroplets for measuring cell forces in living tissues

Mechanobiology – the study of how mechanical forces influence cell, tissue and organ development – is a burgeoning field that involves researchers in biophysics, molecular biology, cell biology and developmental biology, as well as pathologists and physicians. Cells are packed closely together within living tissues, and experience dynamic changes in mechanical forces from neighboring cells and extracellular matrix that push and pull on them, and thereby govern their growth and function. There is high demand among researchers across many fields of biology to measure cell forces, because we know mechanical interactions are critically important during embryo development, tissue repair, fibrosis and cancer development. However little is known about how forces affect cells in vivo because there have been no tools to quantitate forces that cells experience within living, three-dimensional tissues.

To address this challenge, the Wyss Institute at Harvard University has developed a method to directly quantify cell forces in vivo and in vitro using novel microdroplets that provide a direct readout of cellular mechanical force (tension and compression) based on how they are deformed. These cell-sized, fluorescent oil droplets have well-defined mechanical properties and are coated with cell adhesion receptor ligands to allow the droplets to attach to neighboring cells. (Figure 1a) To demonstrate one application, we measured the cell-generated mechanical stresses in living mandibles of mouse embryos. (Figure 1b-d). Droplets that were microinjected between cells in the tissue (Figure 1c) became deformed by local cellular forces (Figure 1d). Changes in these forces can be quantified over time by measuring three-dimensional (3D) deformations in the droplet shape using confocal microscopy, 2-photon or light sheet microscopy combined with simple software algorithms.

The microdroplets can be used in a wide variety of experiments in vivo and within cellular aggregates in 2D or 3D culture in vitro by controlling the type and concentration of ligands on the surface of the droplet, as well as its interfacial tension. This ability to tailor droplet properties makes the technique broadly suited for any study that requires quantification of stresses generated by individual living cells or groups of cells in culture, embryonic tissues, adult organs or diseased tissues. Because of these features, this method could be used in many fields of basic research, and potentially for...
pathological and diagnostic studies.

**Intellectual Property Status:** US provisional application filed.

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