

Automated Liquid Handling

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Automation of 3D Spheroid Production, Cell Culture and Analysis

differentiation, survival, and growth. 3D cell culture, such as 3D microtissues, bridge the gap between traditional monolayer cultures and whole-animal systems, where traditional monolayer and monotypic (2D) cell culture and screening assays do not effectively recapitulate the more complex signaling and cellular interactions found in vivo.

Reproducible cell seeding and reliable formation of similar-sized 3D microtissues is essential to enable collection of robust data when adapting more biologically relevant, complex 3D models to high-throughput workflows. Although seeding of cells, transfer of microtissues, and medium exchange can be performed reliably using automated hand-held pipetting devices, this is not practical when production of large numbers of spheroids is needed for high-throughput studies, necessitating the adaptation of automated liquid handling workflows. Here we demonstrate a standardized, cost effective and automated means of producing and characterizing 3D spheroid microtissues using the InSphero GravityPLUS™ Hanging Drop System and the Zephyr® G3 automated workstation to automate the liquid handling steps involved in microtissue seeding and transfer to the GravityTRAP™ Plate for long-term culture and imaging. Microtissue growth was assessed with the EnSight™ multimode plate reader with well imaging directly in the GravityTRAP™ Plate. A custom-developed analysis method automatically generated brightfield images of each well to identify and measure spheroid area. This allowed for rapid monitoring of microtissue growth without necessitating the addition of a fluorescent label.

Introduction

Advancements in cell culture techniques to more precisely mimic in vivo systems has led to greater interest and utility of three dimensional (3D) cell culture systems, as they represent an improved model for cell migration,

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