3D Cell Culture System to Uncover a Novel Target - In Fibrosis and Other Diseases (Case 2095)

Published date: Dec. 17, 2015

Technology description

Brief Description:

Fibrosis, a prevalent condition where excess connective tissue is accumulated in an organ or a tissue in response to injury, represents a global disease challenge with limited treatment therapies because of the lack of understanding of the disease pathophysiology. Therefore, there is an increase in demand for in vitro models of fibrosis to study debilitating diseases such as pulmonary, liver, and cardiac fibrosis. Three-dimensional (3D) in vitro models can bridge the gap between simplistic 2D culture and animal models to study fibrosis and drug efficacy by creating an in vivo-like microenvironment in a tunable experimental platform. However, current 3D in vitro models that study fibrosis fail to mimic the clinical fibrotic process prior to animal testing and cannot be used for drug screening. Furthermore, high throughput 3D in vitro models are necessary for drug screening, yet development of current 3D in vitro models are time intensive, costly, and difficult to mass produce. For example, recent "Lab-on-a-Chip" technologies aim to mimic a human lung on a microchip that can be used to study diseases such as cystic fibrosis, but production in large quantities for drug testing is not feasible for such complex, dynamic systems as they are extremely costly, require many resources, and are time-consuming to develop.

This invention involves the 3D Petri Dish® technology, created by Jeff Morgan, Professor at Brown University, uses a micro-mold system to create 3D microtissues, termed "spheroids", in the shape of spheres. The micro-mold system uses an agarose solution that is poured into a non-adherent spheroid micro-mold to create agarose hydrogels with a round bottom recess called "microwells". The hydrogel is then removed from the mold and living cells are added in suspension. The cells settle by gravity and adhere to one another to spontaneously self-assemble within 24 hours to form spheroids. These sophisticated 3D spheroids are scaffold-free and conserve the native cell population and extra cellular matrix, unlike current in vitro models that contain unwanted and unnatural structures and require weeks to engineer. Our technology is advantageous over current models, because its simple design can mimic in vivo fibrosis conditions with specific cell types that can be easily analyzed for drug feasibility studies. It can also be mass-produced at a low cost, is easy to use, and can be created in just 24 hours. The model can be tailored in many ways. For example, cell types can be fluorescently labeled before or after fabrication of spheroids for analysis, and drug-efficacy can be tested at different time points within the process.

3D spheroids created by the micro-mold system exhibit capabilities for high throughput assays in drug screening, because they can easily be mass-produced and are cost-effective. Each gel contains 96 microwells, therefore 96 spheroids with tunable cell densities can be created from just one gel. This can significantly reduce time and money spent on complex 3D in vitro models and animal models for initial drug screening assays. In a recent press release at Brown University, 3D spheroids, termed "mini brains" were created from primary cortical neurons using the micro-mold system and were estimated to cost $0.25 cents for each mini brain, confirming the low cost system. This novel technology can also be used as an experimental platform to study fundamental biological questions associated with the pathways and mechanisms leading to scarring during fibrotic process in order to successfully find therapies to treat the disease condition. In this relatively simple, dynamic 3D microtissue system, cell-cell interactions and mechanical forces with spheroids mimicking fibrosis will aid in understanding pathways that lead to the formation of the disease.

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