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ABSTRACT

**Cutting-edge 3D Cell Culture System for Drug Discovery and
Regenerative Medicine**

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NanoCulture Plate (NCP) is a novel experimental system developed for three-dimensional cell culture without any use of gel matrix or matrix-coating. The surface on NCP is covered with a special film with Nano-fabrication. This system enables spheroid formation using conventional cell culture techniques. The spheroids attach to NCP plate by pseudopodia form a round shape that has been confirmed with a scanning electron microscopy (SEM).

The spheroid formation depended on the NCP fabrication patterns, cell culture medium types and cell types. The cell culture conditions for spheroid formation were optimized for more than 50 cell types including cancer cell lines, normal cells and stem cells.

At the molecular level, expression levels of those factors that characterize *in vivo*-like environment were altered in spheroids compared to monolayer culture. The protein expression of HIF-1, VEGF and Akt was significantly increased in the cancer cell spheroids. In addition, 3-D spheroids showed different drug sensitivity which depended on the combination of specific drug and cell types compared to monolayer cells.

NCP can also be used for spheroid formation of normal cells such as hepatocytes, adipocytes, osteoblast and mesenchymal stem cells. On NCP, the characteristics of cellular differentiation were maintained and accelerated compared to monolayer cultured cells. Hepatocytes secreted higher levels of albumin, one of the differentiation markers, and *cytochrome p450* gene expression was upregulated. Moreover, adipocytes accumulated triglyceride (TG). Stem cells form spheroids and differentiate to adipocytes with higher content of TG after inducing differentiation on NCP.

These results suggested that NCP can create an *in vivo*-like environment. Therefore NCP culture system can be employed for *in vitro* drug screening and regenerative medicine research to obtain *in vivo* comparable results.

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