**Large-scale Integrated Platform for Digital Mass Culture of Adherent Cells**

*Dae-Hyeong KimA,B*

ACenter for Nanoparticle Research, Institute for Basic Science

BSchool of Chemical and Biological Engineering

Seoul National University, Seoul 08826, Korea

A platform capable of culturing anchorage-dependent cells in large-scale with fast, efficient, and accurately controlled manner is extremely important in the industrial applications that require large amount of cells, such as personalized cell-therapy and in vitro toxicity testing in pharmaceutical and cosmetic industries. And cellular activities such as proliferation and differentiation during the cell culture, including large-scale cultures, have long been observed by microscopy and/or impedance sensing methods. However, microscopy allows observation of only localized area of the entire cell substrate, which is time-consuming and needs high manpower to monitor entire cells in the large-scale cell culture. The systems using the impedance sensor also have several limitations in multifunctionality, spatial mapping capability, and automatic feedback controllability.

We herein present a large-scale integrated smart culture platform of anchorage-dependent cells. This novel platform technology can digitalize the mass cell manufacturing process to become simple, fast, and highly productive by allowing thorough monitoring of key indicators with high spatial resolution during the cell culture, individual control of cells at specific locations in 3D cell culture space, and in situ maintenance of the cell culture process including culture medium exchange and perfusion, and wireless connectivity of entire cell culture substrates to the central control system.

Our platform is developed by a series of integration methods incorporating arrays of ultrathin impedance, temperature, pH, potassium sensors and electrical and thermal stimulators transfer-printed onto the 3D-printed polylactic acid substrates. These porous and stackable smart sensor/actuator-integrated substrates, which are coated with graphene oxide nanosheets for enhanced cellular adhesion, can be assembled into 3D multilayer stacks for mass culture of various types of cells with high space efficiency. The sensors and stimulators in each stack are interconnected through the wireless system, transmitting signals to and being managed by a central control system wirelessly.

With our system, a single person can control numerous cell culture platforms, automatically acquiring massive amount of data about the cultured cells, and delivering appropriate feedback stimulation and/or media circulation actions in real time to ensure that the cell culture environment is well maintained throughout the culturing process.