

# Open Gradient Exposure Platform for Cell Culture

**A versatile, open lab-on-a-chip platform controls chemical gradients to accurately measure the dose-dependent impact of various substances on cell and tissue response for pharmaceutical research and disease modeling.**

The tissue microenvironment plays a role in normal development and disease and led to the exploration of cell culture approaches to integrate controlled microenvironmental conditions by scientists. The production of chemicals, such as reactive oxygen species (ROS), is frequent in the microenvironment and may lead to oxidative stress, which is present in several pathologies including metabolic disorders, neurodegenerative diseases, and cancer. To assess the impact of ROS on cells requires the measurement of the oxidative DNA damage inside the cells and levels of expression of antioxidant proteins. ROS also triggers changes in nuclear morphology, which is important for the control of cell behavior, including the aggressiveness of cancer cells. For instance, progression from preinvasive to invasive cancer depends on local microenvironmental conditions; hence, the level of ROS might be critical in order to reach a threshold leading to progression switch for certain types of cancers. Therefore, a cell culture system that enables assessing, in the same culture sample, the impact of ROS delivered as a gradient might help sort out relationships among ROS-induced cellular injury, cellular protective response to oxidative stress, and developing phenotypic changes revealed by nuclear morphology.

Purdue University researchers have developed an open gradient exposure platform for creating a gradient of a chemical and/or testing the dose-dependent impact of a chemical, e.g., toxin, drug, ion, and on cells and tissues, by providing a lab-on-a-chip microenvironment. This platform allows for controlled chemical delivery through a paper microfluidic underlayer set up, enabling easy access and analysis of the response of cells and tissues due to the open chamber, unlike the closed microfluidic gradient systems. As a proof-of-concept, Purdue researchers have demonstrated with the gradient-on-a-chip that the level of ROS exposure significantly affects the extent of the cellular response, notably for nuclear morphology, a potential marker of phenotypic changes, and that a same cellular response occurs for

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different levels of ROS depending on extracellular matrix stiffness. These results demonstrate the importance of threshold for the impact of a chemical depending on the initial tissue condition. Changes occurred after only four hours; the use of the gradient-on-a-chip in future studies over several days is possible. This platform progressively acquires a more comprehensive picture of the microenvironmental impact on the response to chemical exposure and is amenable for different cell culture conditions, e.g., standard 2D culture, 3D culture with different matrices.

**Advantages:**

- Measures the microenvironmental impact on the cellular response to chemical exposure
- Measures dose-dependent impact of a chemical on cells
- Allows for testing over longer time periods thanks to continuous renewal of the gradient and cell culture medium
- Recreates chemical homogeneity or heterogeneity of a microenvironment in a controlled manner
- Convenient for gathering cell cultures for additional processing since 2D and 3D cell cultures are done on a paper substrate that can be easily handled
- Allows for cell culture with liquid-air interface
- Provides medium and chemicals from underneath the cells mimicking liquid diffusion to the cells
- Easy to assemble, disassemble, and sterilize

**Potential Applications:**

- Pharmaceuticals R&D-study of microenvironmental exposure linked to disease risk, onset and progression, as well as microenvironmental conditions that influence tissue development

**TRL: 5**

**Intellectual Property:**

Provisional-Patent, 2017-03-30, United States | Utility Patent, 2018-03-29, United States

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