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# Cellular Targeting to Dual Gaseous Microenvironments by Polydimethylsiloxane Microchip

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**Abstract :** We report a microfluidic chip that can be used to modify the gaseous microenvironment of a cell-culture in ambient atmospheric conditions. The aim of the study is to show the cellular response to nitric oxide (NO) under hypoxic (oxygen < 5%) condition. Simultaneously targeting to hypoxic and nitric oxide will provide an opportunity for NO-based therapeutics. Studies on cellular responses to lowered oxygen concentration or to gaseous mediators are usually carried out under a specific macro environment, such as hypoxia chambers, or with specific NO donor molecules that may have additional toxic effects. In our study, the chip consists of a microfluidic layer and a cell culture well, separated by a thin gas permeable polydimethylsiloxane (PDMS) membrane. The main design goal is to separate the gas oxygen scavenger and NO donor solutions, which are often toxic, from the cell media. Two different types of gas exchangers, titled 'pool' and 'meander' were tested. We find that the pool design allows us to reach a higher level of oxygen depletion than meander (24.32 ± 19.82 %vs -3.21 ± 8.81). Our microchip design can make the cells culture more simple and makes it easy to adapt existing cell culture protocols. Our first application is utilizing the chip to create hypoxic conditions on targeted areas of cell culture. In this study, oxygen scavenger sodium sulfite generates hypoxia and its effect on human embryonic kidney cells (HEK-293). The PDMS membrane was coated with fibronectin before initiating cell cultures, and the cells were grown for 48h on the chips before initiating the gas control experiments. The hypoxia experiments were performed by pumping of $O_2$-depleted $H_2O$ into the microfluidic channel with a flow-rate of 0.5 ml/h. Image-iT® reagent as an oxygen level responser was mixed with HEK-293 cells. The fluorescent signal appears on cells stained with Image-iT® hypoxia reagent (after 6h of pumping oxygen-depleted $H_2O$ through the microfluidic channel in pool area). The exposure to different levels of $O_2$ can be controlled by varying the thickness of the PDMS membrane. Recently, we improved the design of the microfluidic chip, which can control the microenvironment of two different gases at the same time. The hypoxic response was also improved from the new design of microchip. The cells were grown on the thin PDMS membrane for 30 hours, and with a flowrate of 0.1 ml/h; the oxygen scavenger was pumped into the microfluidic channel. We also show that by pumping sodium nitroprusside (SNP) as a nitric oxide donor activated under light and can generate nitric oxide on top of PDMS membrane. We are aiming to show cellular microenvironment response of HEK-293 cells to both nitric oxide (by pumping SNP) and hypoxia (by pumping oxygen scavenger solution) in separated channels in one microfluidic chip.

**Keywords :** hypoxia, nitric oxide, microenvironment, microfluidic chip, sodium nitroprusside, SNP
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