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HOLLOW FIBER-BASED LAB-ON-A-CHIP DUAL PERFUSION SYSTEM WITH INTEGRATED FLUORESCENCE-BASED OXYGEN MONITORING

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INTRODUCTION

The development of complex 3D tissue cultures is increasingly gaining importance for both Tissue Engineering and the replacement of animal testing used in the cosmetics and pharmaceutical industries [1, 2]. The maintenance of complex biological 3D microenvironment through an integrated vascular system represents the main challenge.

SETUP

A hollow fiber-based lab-on-a-chip dual perfusion system was developed for cultivation of micro-organoid 3D tissue cultures, which ensures the maintenance of the biological 3D microenvironment with simultaneously protection of possible interactions among different cell types or tissues. For that reason a hollow fiber network was integrated, which acts as artificial vessels. The supply with medium and oxygen is carried out by an attached microfluidic perfusion system that is operated by implemented micro pumps. This bioreactor, which was designed as a lab-on-a-chip system, allows a dual perfusion by integration of several separately arranged microfluidic circuits. A spatial resolved online monitoring system is required to characterize the properties and to monitor the cell culture. Therefore a miniaturized fluorescence lifetime-based measurement technology is presented, which allows a systematic and integrated monitoring of the oxygen consumption during the cultivation.

RESULTS

Based on oxygen-sensitive fluorescent particles, that have been integrated in the fluidic system, the functionality was demonstrated successfully by an artificial enzyme-based oxygen consumer. For this purpose, glucose oxidase (GOD) is used instead of cells. Like shown in figure 2 the measurement can be automated with an XYZ-robot to get the spatially resolution of the oxygen concentration.

[1] M. Baker: "A Living system on a chip", Nature, 471, 664-665, 2011.
[2] U. Marx, et al: "Human-on-a-chip Developments: A Translational Cutting-edge Alternative to Systemic Safety Assessment and Efficiency Evaluation of Substances in Laboratory Animals and Man?", ATLA, 40, 235-257, 2012

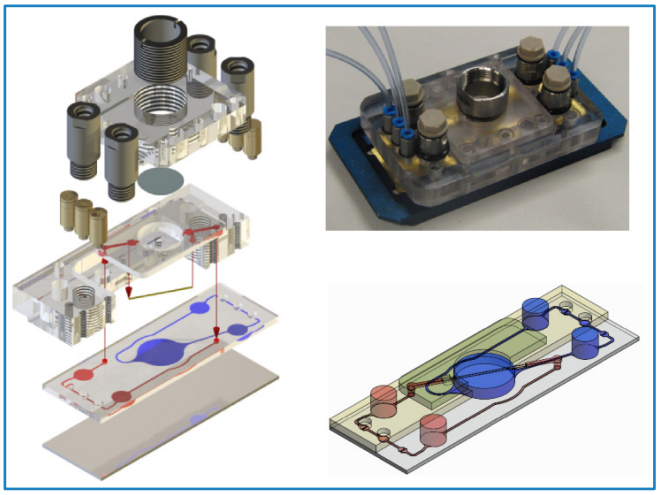

FIG. 1:
Hollow fiber-based lab-on-a-chip dual perfusion system

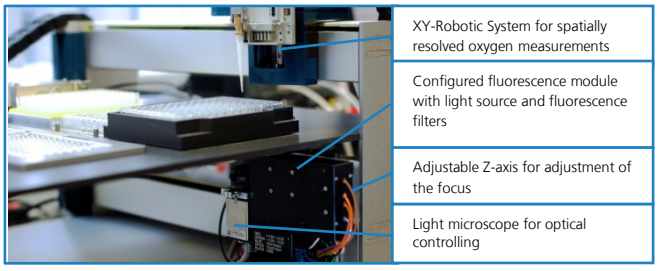

FIG. 2:
Miniaturized automated fluorescence lifetime-based measurement technology

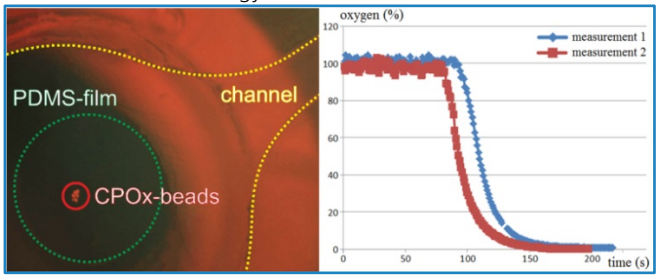

FIG. 3:
Left: Immobilized oxygen-sensitive fluorescent particles
Right: Measured oxygen concentration in the medium during the enzyme catalyzed reaction