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A New Non-Invasive Technique for Measuring 3D-Oxygen Gradients in Wells During Mammalian Cell Culture

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Abstract:

Thyroid is a glandular tissue in the human body in which the function can be severely affected by endocrine disrupting chemicals (EDCs). Current in vitro assays to test endocrine disruption by chemical compounds are largely based on 2D thyroid cell cultures, which often fail to precisely evaluate the safety of these compounds. New and more advanced 3D cell culture systems are urgently needed to better recapitulate the thyroid follicular architecture and functions and help to improve the predictive power of such assays. Herein, the development of a thyroid organoid-on-a-chip (OoC) device using polymeric membranous carriers is described. Mouse embryonic stem cell derived thyroid follicles are incorporated in a microfluidic chip for a 4 day experiment at a flow rate of 12 µL min−1. A reversible seal provides a leak-tight sealing while enabling quick and easy loading/unloading of thyroid follicles. The OoC model shows a high degree of functionality, where organoids retain expression of key thyroid genes and a typical follicular structure. Finally, transcriptional changes following benzo[*k*]fluoranthene exposure in the OoC device demonstrate activation of the xenobiotic aryl hydrocarbon receptor pathway. Altogether, this OoC system is a physiologically relevant thyroid model, which will represent a valuable tool to test potential EDCs.

Keywords: microfluidics, mouse thyroid follicles, organoids, reversible sealing, thermoformed carriers, thyroid functionality