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A microfluidic cell culture device with integrated microelectrodes for barrier studies

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INTRODUCTION

Trans-epithelial electrical resistance (TEER) is one of the widely used and conceivably the most straightforward technique for understanding the integrity of an epithelial or endothelial cell layer (1,2). This paper describes a simple and straightforward fabrication process of microelectrodes in a multi-layer and multi-chamber lab-on-a-chip device for measuring TEER. We propose using a combination of two different metals for fabricating the microelectrodes to acquire TEER measurements in the microdevice: a low melting temperature indium alloy (InBiSn) on the one hand, and platinum (Pt) on the other hand.

FABRICATION OF MICROTOREDEDES

The microfluidic device was fabricated using thin-film 'dry' chemistry (3). The design and fabrication of the microfluidic chip have been reported earlier (4). Two different metals were used to fabricate the microelectrodes. Top electrodes = Platinum wire, Bottom electrodes = Indium-based alloy (InBiSn, in 51%, B 32.5%, Si 16.5% by weight).

RESULTS AND DISCUSSION

BIOCOMPATIBILITY STUDIES WITH INDIUM ALLOY

The biocompatibility of InBiSn was evaluated by culturing Caco-2 cells in the presence of small pieces of the alloy. Phase contrast microscopic images confirmed that the Caco-2 cells cultured in the microfluids containing the InBiSn metal have multiplied. The viability of the Caco-2 cells was further determined with live/dead cell stains. The fluorescent images of the cells showed that the mean cell viability was > 95% in all the microfluids containing the metal (n = 3) (Fig. 2d). The results were comparable to the control microfluids (~ 100% cell viability). As Pt is biocompatible and is widely used in medical devices (5) we conclude that the Pt and InBiSn electrode material are biocompatible.

MICROTOREDEDES FOR SENSING DYNAMIC BARRIER CHANGES

Day 8 Caco-2 cell layers were challenged by the membrane enhancer tetradecyl-β-D-Maltoside (TDM) (7). This resulted in a decrease in TEER values for both Transwell and microfluidic systems (Fig 4a). Further analysis of the disrupted Caco-2 barrier was conducted by immunofluorescence staining of the tight junctions and fluorescence staining of the nucleus (Fig 4b-d).

CONCLUSION

Here, a simple and straightforward procedure for using two different metals to fabricate the microelectrodes in a compact, multi-chamber microfluidic cell culture device for measuring cell barrier function is presented. The metals used for fabricating the microelectrodes were biocompatible and showed capability in measuring TEER across the cells layers. Additionally, the electrodes were capable in sensing dynamic changes to the barrier property when the cells were challenged with a membrane enhancer, Immunofluorescence staining towards the tight junctions of the Caco-2 monolayers was also conducted to further confirm the validity of the TEER measurements. Such a set-up potentially provides a solution to the limited existing equipment for acquiring TEER measurements in compact microfluidic devices for cell culture.

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REFERENCES


