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Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
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 proposed using a combination of two different metals for fabricating the microelectrodes to acquire TEER measurements in the microfluidic low melting temperature indium alloy (InBiSn) on the one hand, and platinum (Pt) on the other hand.

FABRICATION OF MICROELECTRODES

The microfluidic device was fabricated using thin-film ‘‘dial’’ 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 5%, B 32.5%, Sn 16.5% by weight.

RESULTS AND DISCUSSIONS

REAL-TIME TEER MEASUREMENTS

The microfluidic chip with microelectrodes was assembled onto a cell culture platform with MAINSTREAM components (6) and seeded with Caco-2 cells or CT26 cells, respectively. The TEER measurements recorded for the microchambers seeded with Caco-2 cells showed significant increase with time. In contrast, chambers seeded with CT26 cells resulted in an overall low TEER value (Fig. 3).

BIOMCOMPATIBILITY STUDIES WITH INDIUM ALLOY

The biocompatibility of InBiSn was evaluated by culturing Caco-2 cell in the presence of small pieces of the alloy. Phase contrast microscopic images confirmed that the Caco-2 cells cultured in the microfluidics containing the InBiSn metal have multiplied. The viability of the Caco-2 cells was further determined with live/dead cell staining. The fluorescent images of the cells showed that the mean cell viability was > 95% in all the microfluidics containing the metal (n = 3) (Fig. 2d). The results were comparable to the control microfluidic cultures (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.

REFERENCES


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.

ACKNOWLEDGEMENTS

This work is supported by The Danish Council for Independent Research and the Lundbeck Foundation.