Triple co-culture cell model as an in vitro model for oral particulate vaccine systems

Nielsen, Line Hagner; De Rossi, C.; Lehr, C.-M.; Rades, T.; Boyd, B.; Boisen, Anja; Gordon, S.

Publication date:
2016

Document Version
Peer reviewed version

Please create your abstract using the following template and send the document as pdf-file to Biobarriers2016@mx.uni-saarland.de
Please do not modify the format of this template! Abstract limit is 1 page A4.
NOTE: Please save your abstract file according to the name of the presenting author as a 'pdf ' file (Author A B.pdf).

Triple co-culture cell model as an *in vitro* model for oral particulate vaccine systems

Hagner Nielsen L.[1], De Rossi C.[2], Lehr C-M.[2,3], Rades T.[4], Boyd B.[5], Boisen A.[1], Gordon S.[2]

[1]Department of Micro and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark

[2]Department of Drug Delivery, Helmholtz Institute for Pharmaceutical Research Saarland, Helmholtz Centre for Infection Research, Saarbrücken, Germany

[3]Department of Pharmacy, Biopharmacy and Pharmaceutical Technology, Saarland University, Saarbrücken, Germany

[4]Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

[5]Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, Australia

A triple co-culture cell model of Caco-2 cells, dendritic cells and macrophages (Figure 1) has previously been developed for studying intestinal permeability in a state of inflammation [1],[2].

The aim of this study was to investigate the applicability of this cell model for testing the immunostimulatory ability of particulate vaccine formulations designed for oral delivery. Levels of cytokine production in response to vaccine administration were measured following particulate vaccine administration, as an indication of dendritic cell and macrophage activation. Precursors of cubosomes containing the model antigen ovalbumin was spray dried to obtain a particulate vaccine model system for testing in the cell model. The precursors were shown to form cubosomes when dispersed in aqueous medium, and was therefore used as the vaccine formulation for testing on the co-cultures.

After 11 days, the TEER values of the co-cultures were found to be 860-1340 $\Omega \cdot cm^2$; the formulations were incubated with the co-cultures at this time point. From confocal microscopy images, it was observed that the THP-1 cells (macrophages) migrated into the overlying Caco-2 cell monolayer when the co-cultures were incubated with particle formulations. This was not the case when incubating with ovalbumin solution or blank. The ELISA screening assay showed production of a wide range of cytokines following culture incubation with cubosomes (with and without ovalbumin) and LPS solutions, indicative of a stimulatory effect; this was not observed with ovalbumin and blank solution. An example of the results is shown in Figure 2 for IL-17A.

An established co-culture of Caco-2, THP-1 and MUTZ-3 cells showed promise as an *in vitro* model for testing of oral vaccine formulations. Mobility of co-culture immune cells as well as cytokine production observed following treatment with spray dried cubosomes as a particulate vaccine formulation will be further investigated.

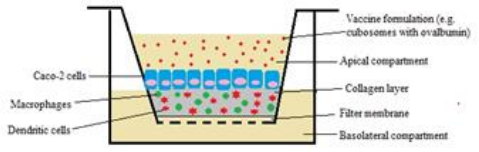

Figure 1: Schematic of the triple co-culture model being adapted for oral vaccine delivery.

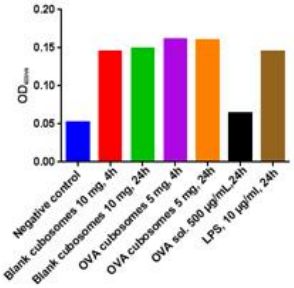

Figure 2: An example of cytokine production of IL-17A after Incubation of formulation with the co-cultures for 4 or 24h.

Acknowledgments:

The authors would like to acknowledge the Danish Research Council for Technology and Production (FTP), Project DFF - 4004-00120B for financial support. Moreover, the Danish National Research Foundation, project: DNRD122 is acknowledged.

References:

1. Leonard, F., Collnot, EM., Lehr, C-M.: *Mol Pharm*. 2010, 7: 2103-2119.
2. Susewind, J. et al.: Nanotoxicology, 2015, 4: 1-10.