3D lung epithelial models to study host-pathogen interactions

Commonly used acronym: *3D lung models*

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Translational - Applied Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	alveolar epithelial cells, bronchial epithelial cells from patients with lung disease or healthy individuals

DESCRIPTION

Method keywords

in vivo-like models

organotypic

host-pathogen interactions

inflammation

Pseudomonas aeruginosa

microbiome

cytotoxicity

host-associated biofilms

preclinical drug development

antibiotic activity

Scientific area keywords

microbiology

antibiotics

cystic fibrosis

Chronic obstructive pulmonary disease

infectious disease

biofilm

lung disease

Method description

Three-dimensional (3D) lung epithelial cell models mimic key aspects of the parental tissue, including apical-basolateral polarity and barrier function (Barrila et al. 2010, PMID: 20948552). These 3D cultures are generated using the rotating wall vessel (RWV) bioreactor system, allowing host cells to grow and differentiate on porous ECM-coated microcarrier beads in an optimized suspension culture. Upon differentiation, cultures can be transferred into multi-well plates, to enable targeted throughput and high reproducibility. 3D lung cell cultures can be applied to study various aspects of the infectious

disease process, enabling to evaluate both host and bacterial behavior during host-pathogen interactions under physiologically relevant conditions. The developed models are also useful for testing new or existing antimicrobial agents, as bacterial susceptibility to antimicrobials is different in the 3D lung models compared to conventional assays (Crabbé et al. 2017, PMID: 28256611; Rodriguez-Sevilla et al. 2018, PMID: 29648588; Grassi et al. 2019, PMID: 30800115; Crabbé et al. 2019, PMID: 31034512).

Lab equipment

In addition to basic cell culture equipment, specialized bioreactors are needed to generate the described 3D lung cell cultures.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- *In vivo*-like characteristics ;
- Targeted throughput ;
- High reproducibility.

Challenges

- More expensive than conventional (2D) assays ;
- Expertise and equipment needed.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Barrila J., A. Radtke, A. Crabbé, S.F. Sarker, M.M. Herbst-Kralovetz, C.M. Ott and C.A. Nickerson (2010). Organotypic 3D cell culture models: using the rotating wall vessel to study host-pathogen interactions. Nature Reviews Microbiology 8(11): 791-801.

Crabbé A., M.A. Ledesma, and C.A. Nickerson (2014). Mimicking the host and its microenvironment in vitro for studying mucosal infections by Pseudomonas aeruginosa. Pathogens and Disease 71(1): 1-19.

Crabbé A, Liu Y, Matthijs N, Rigole P, De La Fuente-Nùñez C, Davis R, Ledesma MA, Sarker S, Van Houdt R, Hancock RE, Coenye T, Nickerson CA (2017). Antimicrobial efficacy against Pseudomonas aeruginosa biofilm formation in a three-dimensional lung epithelial model and the influence of fetal bovine serum. Scientific Reports. 3;7:43321.

Rodríguez-Sevilla G, Rigauts C, Vandeplassche E, Ostyn L, Mahíllo-Fernández I, Esteban J, Peremarch CP, Coenye T, Crabbé A (2018). Influence of three-dimensional lung epithelial cells and interspecies interactions on antibiotic efficacy against Mycobacterium abscessus and Pseudomonas aeruginosa. Pathogens and Disease. 76(4).

Grassi L, Batoni G, Ostyn L, Rigole P, Van den Bossche S, Rinaldi AC, Maisetta G, Esin S, Coenye T, Crabbé A (2019). The Antimicrobial Peptide lin-SB056-1 and Its Dendrimeric Derivative Prevent Pseudomonas aeruginosa Biofilm Formation in Physiologically Relevant Models of Chronic Infections. Frontiers in Microbiology. 8;10.

Crabbé A, Ostyn L, Staelens S, Rigauts C, Risseeuw M, Dhaenens M, Daled S, Van Acker H, Deforce D, Van Calenbergh S, and Coenye T (2019). Host metabolites stimulate the bacterial proton motive force to enhance the activity of aminoglycoside antibiotics. PLOS Pathogens 15(4): e1007697.

Van Acker H, Crabbé A, Jur?nas D, OstynL, Sass A, Daled S, Dhaenens M, Deforce D, Teirlinck D, De Keersmaecker H, Braeckmans K, Van Melderen L, and Coenye T (2019). The role of mini-proteins in Burkholderia cenocepacia J2315 biofilm formation and persistence. Biofilms (1), 100001.

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