REFERENCE NUMBER TO 01-01011

Biphasic, copolymeric, stretchable membrane and bioreactor for investigating cells at the air liquid interface (ALI)

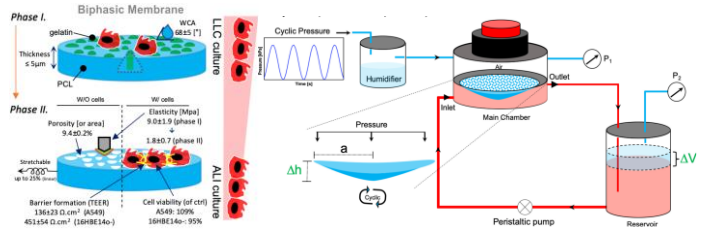
Keywords: cells, culturing lung epithelial cells, air liquid interface, ALI, CIVIC, bioreactor, bi-phasic, stretchable, membrane, copolymers, gelatin, PCL

INVENTION NOVELTY

Here, we introduce a novel biphasic copolymeric membrane suitable for investigating lung cells in a bioreactor simulating physical conditions by stretching the membrane due to air pressure changes. The membrane consists of poly(ε-)caprolactone (PCL) and gelatin resembling the main characteristics of the alveolar basement membrane. It can be realized with a thickness of 1 to 5 µm and stretchability up to 25% or even 40% linear strain. Furthermore, the membrane offers surface wettability and porosity for culturing lung epithelial cells under air-liquid interface conditions. Integrated into a stretch-activated lung bioreactor it allows to investigate the effect of cyclic mechanical stretch on cell physiology and the transport of nanoparticles, drugs or toxins.

VALUE PROPOSITION

Chronic respiratory diseases are among the leading causes of death worldwide, but so far only symptomatic therapies are available for terminal illness. This in part reflects a lack of biomimetic *in vitro* models that can imitate the complex environment and physiology of the lung. This Biphasic Elastic Thin for Air-liquid culture conditions (BETA) membrane facilitates cell adhesion and proliferation without pre-treatment of the membrane and provides sufficient porosity and biomimetic elasticity required for *in vitro* cell-stretch applications under ALI culture conditions. Combined with a corresponding bioreactor this membrane offers considerable advantages over currently used systems and may contribute to true biomimetic *in vitro* models of the lung for translation of *in vitro* response studies into clinical outcome.



Biphasic membrane changes its characteristics synchronized with the change in requirements for the initial cell growth phase versus subsequent cell-stretch experiments with an Cyclic In VItro Cell-stretch (CIVIC) sytem, see furhter reading.

TECHNOLOGY DESCRIPTION

The biphasic membrane sequentially adapts its properties providing optimum characteristics for initial cell growth (phase I) and biomimetic properties for cyclic cell-stretch experiments (phase II). It is manufactured by spin-coating of a copolymer emulsion consisting of PCL and gelatin. Gelatin creates a smooth and non-porous membrane and mediates cell attachment in phase I. As cells proliferate, they secrete their own ECM allowing them to gradually migrate into the PCL regions, forming a confluent cell layer. Moreover, water-soluble gelatin serves as a sacrificial polymer which is gradually dissolved in cell culture medium, inducing porosity in the originally non-porous membrane as required for phase II. The selective removal of gelatin increases the elasticity of the membrane to a value typically observed for lung and required for the cell-stretch experiments under ALI culture conditions in a stretch activated bioreactor in phase II.

COMMERCIAL OPPORTUNITY

The technology is available for in-licensing.

DEVELOPMENT STATUS

Membrane fabrication methods, cell culture and bioreactor setups for *in vitro* cell measurements have been established.

PATENT SITUATION

A priority claiming European patent application was filed in 2020.

FURTHER READING

A Biomimetic, Copolymeric Membrane for Cell-Stretch Experiments with Pulmonary Epithelial Cells at the Air-Liquid Interface; Ali Doryab, et. al.; Adv. Funct. Mater. 2021, 31, 2004707.

A Bioinspired in vitro Lung Model to Study Particokinetics of Nano-/Microparticles Under Cyclic Stretch and Air-Liquid Interface Conditions; Ali Doryab, et. al.; Front. Bioeng. Biotechnol. 9:616830.

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