Alveolar mimics with periodic strain and its effect on the cell layer formation

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Abstract

We report on the development of a new model of alveolar air-tissue interface consisting of an array of suspended hexagonal monolayers of gelatin nanofibers supported by microframes and a microfluidic device for the patch integration. The suspended monolayers are deformed to a central displacement of 40-80 μm at the air-liquid interface by application of air pressure in the range of 200-1000 Pa. With respect to the diameter of the monolayers that is 500 μm, this displacement corresponds to a linear strain of 2-10% in agreement with the physiological strain range in the lung alveoli. The culture of A549 cells on the monolayers for an incubation time 1-3 days showed viability in the model. We exerted a periodic strain of 5% at a frequency of 0.2 Hz during 1 hour to the cells. We found that the cells were strongly coupled to the nanofibers, but the strain reduced the coupling and induced remodeling of the actin cytoskeleton, which led to a better tissue formation. Our model can serve as a versatile tool in lung investigations such as in inhalation toxicology and therapy.

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(a) Nanofibers Microframe
(c) Pressure Displacement
Radius
Bare gelatin nanofibers
Pressure
Displacement
A549-seeded culture patch
Pressure (Pa)
Time (s)
Patm
Pmax
(b) 3

(b) Pressure (Pa) Time (s)
Bare gelatin nanofibers  Pressure  Radius  Displacement
AS49-seeded culture patch  Pressure  Displacement

3
(a) i) $w = 0 \, \mu m$

ii) $w = 35 \, \mu m$

iii) $w = 70 \, \mu m$

(b) 120

Relaxed, 0 µm
Half-depth, 35 µm
Full-depth, 70 µm
Theory

(c) 140

AS49-cultured membrane

Experiment

Bare gelatin membrane

Displacement (µm)
Radial Distance (µm)
Pressure (Pa)
Displacement (µm)
0 400 800 1200 1600

Data may be preliminary.
(a) $Z=0$ (out-plan) $+3 \mu m$ $+6 \mu m$ $+10 \mu m$ (out-plan)

(b) $Z=0$ (out-plan) $+3 \mu m$ $+6 \mu m$ $+10 \mu m$ (out-plan)
Maximum Intensity

Boom

1-day 3-day

Boom

(Mean Intensity)

No strain

Strain

Central

Peripheral

Central

Peripheral

Central

Peripheral

1-day 3-day

Strain

(+)

Roundness

8