

Multi-Parametric, Multi-Cell Barrier Integrity Analysis on Membrane-Based Biochips

Multi-parametric, multi-cell barrier integrity analysis uses a novel combination of TEER and impedance spectroscopy within and on membrane-based biochips. Such endothelialised microchips with controllable permeability facilitate important tools when evaluating nanoparticle translocation across endothelial cell layers, i.e. atherosclerotic endothelium.

BACKGROUND

Microfluidic chips are unique *in vitro* test systems, which combine tissue-mimetic cell culture and microperfusion. They represent powerful tools for controlling the complete cellular microenvironment and for monitoring microvascular permeability at the (sub-)cellular level. Thereby, the translocation of therapeutic or diagnostic nanomaterials can be intensely studied in various diseases, including cancer and atherosclerosis.

TECHNOLOGY

The new method, for the first time, enables a versatile interconnection of multiple electrodes on a single chip. Thereby, highly interdigitated metal thin film electrodes of a defined geometry down to 2.5 μm can be reliably structured on even 10 μm thick flexible porous and free-standing polymeric membranes. The biochip itself is based on fluidic layers fabricated from polydimethylsiloxane or other polymers and a polymeric membrane (polyethylene terephthalate), which carries electrodes, bonded to the fluidic layers. Polyvinyl alcohol is used as a water-soluble mounting layer during fabrication, thus avoiding membrane-damaging solvents. Quintessence is the ability to correlate cell surface coverage using membrane-integrated metal thin film electrodes (2-point impedance measurement setup) with barrier integrity and tightness based on trans-cellular resistance measurements (TEER; 4-point measurement setup). Thus, multiple cell barriers can be probed within a single multi-layered device, allowing electro-analytical biosensing of cell barriers, up to quadruple co-culture.

Indeed, the novel system allows to investigate the impact of (bio)chemical and mechanical stimuli on organ and tissue models, but shows particular significance for studying transvascular permeation of nanoparticles across the permeable endothelium. Respective endothelialised microfluidic chips offer controllable permeability and probing of nanoparticle translocation across endothelial cell layers. Thereby, nanoparticle targeting and accumulation in various disease states, such as atherosclerosis, can be assessed in unprecedented manner.

ADVANTAGES

- Reliable and simple fabrication of microelectrodes on porous membranes, enabling ultrasound assisted lift off
- Monitoring various combinations of cell barriers and cell layers using different electrode sensing circuits based on multiple thin film electrodes (3 x 2 electrodes on 3 planes)
- Generation and analysis of cell barrier models on chip using non-invasive multi-parametric read-out
- Combined study of cell barrier integrity/ formation (TEER) and cell surface coverage/ viability (electrical impedance spectroscopy)

REFERENCE:

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APPLICATIONS:

Thin film, microfluidics, impedance spectroscopy

KEYWORDS:

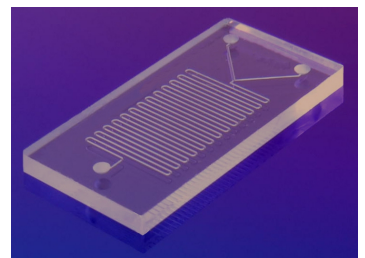
Nanotechnology
Cardiovascular disease
Microfluidics
Non-invasive imaging
TEER measurements

IPR:

EP and US pending

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