How to Cite: Kanabekova, P., Martin, A., Kemelbekova, A., & Kulsharova, G. (2022) Applications of Nanofier Membranes in Microphysiological Systems. *Bulletin of the University of Karaganda – Chemistry, 107(3), 56-66.* https://doi.org/10.31489/2022Ch3/3-22-12

Review Received: 31 May 2022 | Revised: 30 June 2022 | Accepted: 1 July 2022 | Published online: 18 July 2022

UDC 544.42+519.242.7 https://doi.org/10.31489/2022Ch3/3-22-12

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Applications of Nanofiber Membranes in Microphysiological Systems

Microfluidic organs-on-chips or microphysiological systems (MPS) are promising tools that can potentially replace animal testing in drug development. MPS are platforms with microchannels seeded with certain organ cells used to emulate in vivo environments in laboratory conditions. Among them, platforms seeded with lung cells called lung-on-chip devices can evaluate the influence of toxic particles, gases, and chemicals on lung tissue in vitro. Lung-on-chip devices allow the mimicry of healthy lung conditions and a wide range of diseases (asthma, cancer, autoimmune, infections). This review focuses on the use of electrospun nanofiber membranes as a functional basement membrane which plays a central role in the development of lung-on-a-chip platforms. Here, we briefly introduce microfluidic devices, MPS, and lung-on-chip devices. Existing basement membrane models, such as thin-film and gel-based membranes, and their challenges/disadvantages are discussed. Next, the concepts of electrospinning and nanofiber membranes are introduced. Finally, the nanofiber membranes used in lung-on-chip devices are reviewed. Implementation of different polymer materials used to synthesize the nanofiber membranes and different methods for incorporation of the membrane inside the device are discussed. Electrospun nanofiber membranes provide good mechanical properties, allow transmigration of the immune cells, and withstand the physiological strain without affecting the cell viability.

Keywords: microfluidics, microphysiological, nanofiber, basement membrane, electrospinning, lung-on-chip, polycaprolactone, adherent junction.

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Kemelbekova Ainagul is a PhD candidate of materials science. Currently, she is an assistant at the K.I. Satpayev Kazakh National Technical University and a junior researcher at the Institute of Physics and Technology. Her research interests cover nanofiber membranes in micro physiological systems, solar cells. She is actively engaged in scientific research and is working on a dissertation.

Content

Review Plan

Inclusion and Exclusion Criteria: The present review is focused on use of nanofiber membranes as basement membrane in lung-on-chip microfluidic devices.

The review is limited to publications done on lung-on-chip devices in English language. Only articles in microfluidic area were analyzed from sources like Google Scholar, Scopus. The keywords listed above were used in a search of relevant papers. The resultant articles were included to the review. No statistical or correlational analysis was used.

Introduction

Microfluidics can be represented by controlled fluid flow through microstructures or microchannels etched or molded into different material substrates (glass, polymer, silicon). There are various applications of microfluidic devices including material synthesis, molecular analysis, cell studies, drug toxicity, etc. These applications make microfluidics a rapidly developing and promising area in research [1]. One of the applications of microfluidics, organ-on-chip technology, allows mimicry of physiological systems through miniaturized and microscale designs. The mimicry is achieved by designing channels repeating structures within the organs and controlling the significant parameters within the device. Among the parameters, the concentration gradient within the fluid, diversity of cells and their patterning, interactions, fluid, shear forces, and others can be adapted to affect the functionality and characteristics of the device [2]. Conventional 2D cell culture techniques cannot replicate the microphysiological patterns because of their flat nature. Additionally, animal testing does not fully replicate human tissue and raises an ethical issue. Therefore, organ-on-chip platforms have great potential in drug development and toxicology [2].

Currently, a wide range of organ-on-chips for mimicking respiratory, kidney, cardiovascular, pancreatic, gastrointestinal, and neural tissues exist. The concept of ‘body-on-chip’ combining multiple organs is being introduced to develop a system for the complex evaluation of pharmacokinetics and pharmacodynamics of drugs [3]. Within the scope of this review, lung-on-chip models are reviewed. Lung-on-chip devices can be designed to represent healthy and diseased tissues. The design of lung tissue focuses on creating a device that would replicate a mechanically active alveolar-capillary interface with a functional basement membrane (BM) [4–6]. Among the diseases designed on-chip are pneumonia [7, 8], chronic obstructive pulmonary disease (COPD) [9], asthma [10, 11], tuberculosis (TB) [12], lung cancer [13–19], and cystic fibrosis [20, 21]. To simulate a diseased state, ‘healthy’ tissues are treated with chemicals and/or particles that induce pathological changes.

As in many other organ-on-chip devices, the lung-on-chip platforms can use the primary cells, stem cells, and human cell lines. Human cell lines are alveolar epithelial cells, which carry the transport of gases and nutrients. For example, adenocarcinomic cells such as A549 are commonly used [22]. They are easy to use and can be manipulated to induce mutations related to disease conditions such as cystic fibrosis. However, the main limitation is their transformation to immortalize, which is a principal difference from healthy airway cells [23]. The possibility to use primary human cells makes lung-on-chip devices an excellent tool in personalized medicine for drug sensitivity studies. However, the main limitation of using primary cells is their limited proliferative capacity [22]. In turn, preparing lung cells from stem cells is more difficult, which requires different growth and differentiation factors, but they are excellent in replicating human tissue because controlled differentiation induces the expression of proteins and structures as in desired one [24]. Lung tissue besides epithelial and vascular cells includes a wide variety of cells, such as mesenchymal, immune, and smooth muscle cells essential for breathing action, and neurons that control breathing [25]. Combination and diversity of cells, a complicated morphology, and relation to other organ systems make it difficult to replicate lung tissue using conventional cell culture techniques, therefore microfluidic devices might aid in overcoming the challenges related to recapitulating microstructures.

1 Lung-on-chip microfluidic device

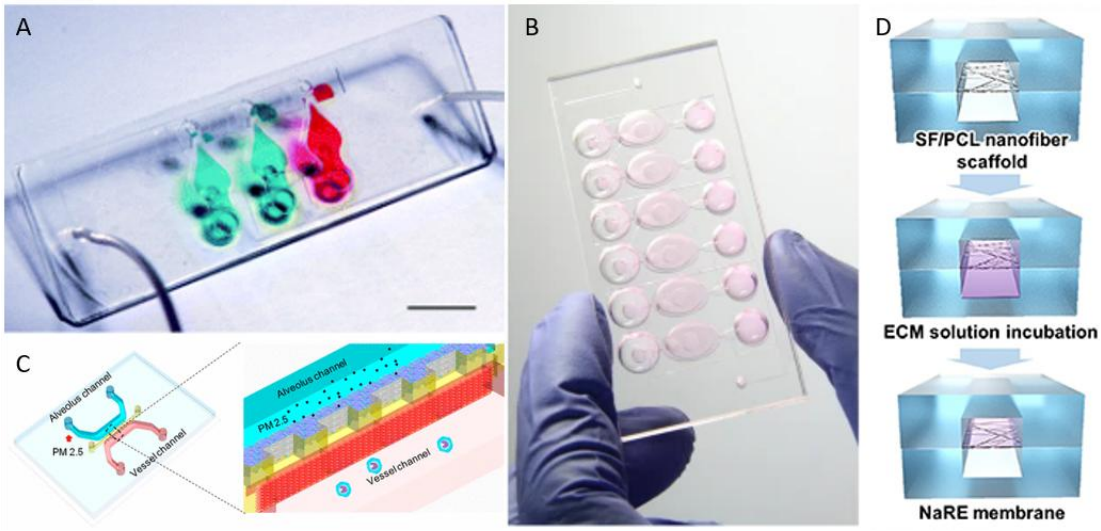
The lung-on-chip devices mimic the basic functional unit of the lung, an alveoli-capillary barrier. Thin layer of pneumocytes and endothelial vascular cells separated and connected by basement membrane is the place where the oxygen/carbon dioxide exchange takes place. In the design of lung-on-chip, scientists rely on the very first lung-on-chip device suggested by Huh in 2010 [4]. It was a two-chamber system, separated by polydimethylsiloxane (PDMS) thin layer. Each chamber represented air and blood compartments respectively, while PDMS functioned as basement membrane [4]. In designing the microphysiological devices, repeating the biomechanical signaling and forces within platform is crucial. For example, the elastic modulus in alveoli tissue is approximately 5 kPa and the expansion of alveoli during the calm breathing reaches only 4% of primary length with alternations of those values in diseased conditions [26]. The strain reaches 12% during deep inspiration, but it is important to note that alveolar distension is not uniform, so strain in some areas can increase to 30%. Besides, other parameters are also important, for example during the breathing the lung tissue stretches and recoils approximately 12 times per minute [27]. Therefore, devices that incorporate the flow are known to be more representative of organ structure than static models [28]. These characteristics are crucial in functionality, timely metabolic exchange and support of the lung tissue itself.

Basement membrane (BM) is a type of extracellular matrix that can be found around many tissues. In lungs, it lies between the epithelial lung and vascular cells. BM is specific for different tissues and has different roles, in alveolar tissues it maintains epithelial cells, facilitates gas exchange, and is involved in immune response [29]. The main components of the BM are proteins that provide elastic/plastic properties and strength: collagen, elastin, proteoglycans [26]. The changes in composition of the basement membrane are common in a wide range of diseases including autoimmune conditions, cancers and inflammatory diseases [30]. Collagen is one of the most abundant proteins, which forms the network of fibrils, aiding in resisting forces and providing tensile strength. In turn, elastin is responsible for elastic properties and stretchability of the BM [27]. Those proteins undergo remodeling in disease conditions, resulting in misbalance and dysregulations in functioning of the BM. In mimicking the BM for lung-on-chip the mechanical characteristics described above are important along with chemical properties of the material such as hydrophobicity, biocompatibility and physical structure that ensure its functionality.

2 Existing lung-on-chip basement membranes

A thin layer of PDMS separating the air and fluid compartment, which was prepared by the microstructuring-lamination process, was cyclically stretched in a breathing manner in a lung-on-chip device developed by Stucki as shown in Figure 1A [31]. The integrity of protein meshwork and thus permeability of BM was not disrupted during ‘breathing’ and the stretch increased the metabolic activity of the cells, enhancing the gas exchange function [31]. Later, the authors suggested a new PDMS-membrane-based device, shown in Figure 1B, which maintained cells for 3 weeks without an external perfusion system [32]. Although PDMS is elastic, not toxic for cells, has pores for the transport in between layers, and was frequently used as BM in lung-on-chip, some disadvantages make it not an ideal candidate. Most of the recent research mentions the ability of PDMS to absorb small molecules, which affect the biochemical microenvironment within the microfluidic device [33]. Other examples of porous membranes that are used to separate air and fluid compartments are polycarbonate (PC) and polyethylene terephthalate (PET). However, the authors mention the main disadvantage of using these membranes as the recreation of a 2D flat surface, which does not fully recapitulate the curvature of alveoli [6]. As a result, a microcurved 3D microfluidic device was designed to conserve the spatial configuration of the lung functional unit. Although the epithelial and endothelial cells were maintained within the device for 2 weeks with features and topography similar to real lung tissues, the mimicry of breathing movement was impossible due to the lack of elastic properties [6].

The BM can be ‘synthesized’ by preparing layer of ‘gel’, which would accommodate cells and mediate the signaling and communication between them. For example, Huang et al. [5] synthesized hydrogel from gelatin methacryloyl (GelMA), while Xu et al. used commercial Matrigel sandwiched between PDMS layer as shown in Figure 1C [34]. In both experiments, the BM maintained its barrier function and some cell experiments were conducted to evaluate the functionality of the devices. The gel-based BMs enhanced recapitulation of microphysiological structures due to its primary 3D nature, so cells maintained the characteristics such as adherent junctions in accordance with histological features of lung tissue. However, the disadvantage of working with hydrogels is the inability to mimic stretchable properties and strain as in ‘breathing’ [33].



A — PDMS based lung-on-chip with thin PDMS basement membrane [31];
B — PDMS based lung-on-chip with PDMS based BM without external perfusion system [32];
C — PDMS based lung-on-chip with Matrigel BM [34];
D — PMMA based lung-on-chip with Nanofiber-Reinforced membrane [35]

Figure 1. Lung-on-chip device models

Another example of the BM mimicry was formed by drop-casting the solution of collagen and elastin on golden mesh in PDMS based microfluidic device, which revealed significantly less absorption of small molecules, with mechanical properties close to physiological 4 kPa elasticity modulus and cause 10 % mechanical strain [33]. Moreover, authors mention that golden mesh structure recapitulates the geometric structure, while the collagen and elastin are natural and biodegradable. Next, BM can be recapitulated using the nanofiber membranes sandwiched in device between polymethyl methacrylate (PMMA) layers as shown in Figure 1D [35]. Nanofiber membranes as a focus of this review will be explained in the next section.

3 Nanofibers in microfluidic systems

Nanofiber membranes show the potential in becoming a better alternative to the conventional membranes in microfluidic systems. Electrospun nanofiber membranes possess a high surface area, a highly porous and interconnected structure that is closer to resembling the basement membrane and extracellular matrix (ECM) of tissues [35, 36]. These unique properties support and facilitate the attachment and migration of cells on the scaffold [37]. The high porosity of the nanofibrous membrane allows more efficient nutrient and waste exchange that further contributes to improved cell proliferation [38]. Even though a simple coating of the conventional membranes with ECM proteins improves cytocompatibility, it is unable to create a 3D topography of the cellular microenvironment [39]. In comparison, during the electrospinning of the nanofibers, proteins can be integrated within the polymer solution reducing fabrication steps and allowing a more homogeneous distribution of proteins throughout the scaffold enhancing its resemblance to the native ECM in tissues [37].

The electrospinning technique is a relatively straightforward process. Electrospinning utilizes high voltage applied to a polymer solution to generate fibers that are deposited on a grounded collector plate. High voltage is required to overcome the surface tension of the polymer solution and induce its transformation into a jet. This facilitates stretching of the polymer chains and evaporation of the solvent, which allows the collection of dry nanofibers. The electrospinning process involves multiple variables that may influence the quality of the nanofibers assessed by their interfiber porosity, fiber morphology, and topography. These variables include conductivity, dielectric constant and surface tension of the solution, molecular weight and structure of the polymer, compatibility of the polymer and solvent, solvent evaporation rate, and solution viscosity. In addition, process settings, such as voltage, flow rate, distance from the needle tip to collector, temperature, and humidity also play an essential role in the suitability of the final solution to be electrospun into dry and homogeneous fibers [40–42].

In microfluidic systems, nanofibrous membranes can be used as bioanalytical systems and organ-on-chip models [43]. Their high surface area enhances the sensitivity of bioanalytical systems through increased

surface functionalization. Examples of such systems include the immobilization of antigens or antibodies for developing immunoassays similar to ELISA assay [44]. In such a system, PLGA and PLA nanofibers showed superior properties to PDMS membrane in immobilizing proteins due to the presence of carboxyl groups on their surface [45]. Moreover, nanofibrous microfluidic systems are also researched for detection of *Escherichia coli* [46], HIV [47], metalloproteinase-9 [48], opium alkaloids [49], cancer biomarkers [50], and circulating tumor cells [51, 52]. These nanofibrous microfluidic systems also hold great potential in molecular diagnostics and screening for therapeutic agents [53].

4 Nanofibers in organ-on-chip models

The unique resemblance of nanofibrous membranes to the native tissue ECM allows their use in organ-on-a-chip models [54]. Electrospun nanofibrous membranes may allow the use of exceptionally thin thickness close to that of a basement membrane in tissues. However, in comparison to conventional membranes such as PDMS, electrospun fibrous membranes may exhibit lower tensile strength and may be too fragile. During sealing procedure of the microfluidic chip, the roughness of the nanofibrous membrane surface may reduce the bonding efficiency and the membrane may get deformed in the process [37, 43], eventually leading to leakage. Nevertheless, due to the previously mentioned limitations of the conventional PDMS membranes, developing electrospun nanofibers are actively researched as an option to mimic the native cellular microenvironment in tissues [55].

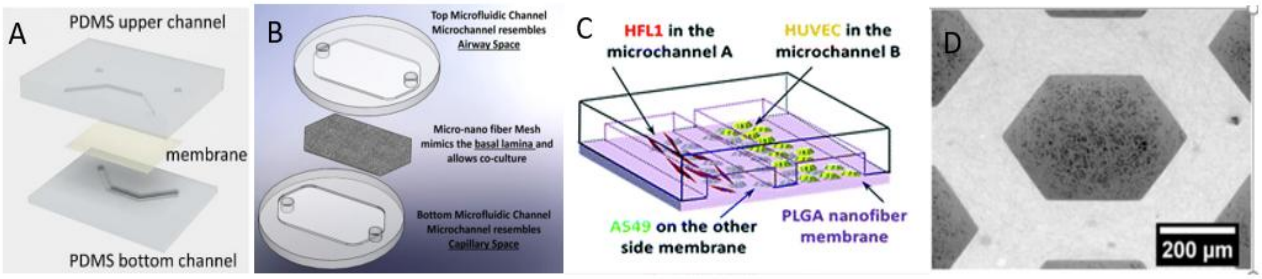
One of the initial *in vitro* models with electrospun membranes studied mimicry of cellular microenvironment using nanofibrous membranes in a microfluidic system [56]. For this purpose, polyurethane in dimethylformamide and tetrahydrofuran mixture was electrospun onto an aluminum foil. The hydrophobic surface of the membrane was treated with acrylic acid to introduce carboxyl and carbonyl group for better cell adhesion and proliferation. This treatment led to lower contact angles and reduced hydrophobicity of the material. In comparison to untreated controls, seeded human mesenchymal stem cells demonstrated better proliferation on the acid-treated membranes. However, this method did not compare nanofibrous membranes to PDMS membranes and the surface treatment of the nanofibrous membrane introduced additional fabrication step.

Later, liver-on-chip models using electrospun nanofibrous membrane were developed from PCL dissolved in chloroform [57]. This membrane was placed on the bottom of the microfluidic chamber. The hepatic carcinoma cells HepG2 were cultured on top of the membrane and showed excellent viability for 14 days. Here, they demonstrated real-time measurements of albumin and alpha-fetoprotein using an ELISA assay. This model utilized nanofibrous membranes collected on the aluminum foil and was not directly electrospun onto the chip.

In comparison, Chuchuy, Rogal [37] demonstrated a proof-of-concept study with the possibility of the electrospun polymer solution of PLA and PLA with GelMA in hexafluoroisopropanol (HFIP) directly onto the microfluidic chip. To create more oriented nanofibers, aluminum foil was placed on the opposite sides of the microfluidic chip. To ensure electrospinning of the nanofibers only to the chip surface, the area around it was sealed with a non-conductive tape. The deposited membrane was then cut to shape using a solvent-wetted scalpel. The comparison between pure PLA and GelMA-PLA fibers demonstrated that during the process of thermal fusion bonding, the membranes exhibited deformation on the edges, changes in fiber diameter, and reduction in membrane size. In contrast, GelMA-PLA nanofibrous membranes were more heat-resistant and remained flat during bonding, but showed slight sagging. Additionally, endothelial and epithelial cells performed better on the gelatin-containing PLA nanofibrous membranes due to the innate cell-recognizing motifs in gelatin, whereas pure PLA membranes required a time-consuming coating process to improve cell adhesion and proliferation.

5 Nanofibers in lung-on-a-chip models

Several studies used PCL-based nanofibrous membranes for lung-on-chip models [39, 58, 59]. A study by Tas, Rehnberg [39] used a commercially available PCL membrane to simulate clinical ventilator-induced lung injury by applying 25 % of mechanical strain on the cell-seeded membrane (Figure 2A). Here, PCL nanofibrous membrane was selected for its good mechanical properties that withstand higher mechanical strain in comparison to natural polymers such as collagen.



A — PCL nanofibrous membranes for simulating ventilator-induced lung injury [39];
B — Gelatin-containing PCL nanofibrous membrane for simulating alveolar-capillary barrier [58];
C — PLGA nanofibrous membrane for simulating alveolar respiratory membrane [62];
D — Gelatin nanofibrous membranes for simulating alveolar air-tissue interface [63].

Figure 2. Incorporation of nanofibrous membranes into microfluidic device for lung-on-chip models

A couple of other studies simulated an alveolar-capillary barrier using electrospun PCL nanofibrous membranes [58, 59]. Different ratios of PCL and gelatin in HFIP solution were used to electrospun nanofibrous membranes that were bound to the layers of the microfluidic system *via* oxygen plasma treatment (Figure 2B). A higher ratio of gelatin to PCL in the nanofibers led to an increase in fiber diameter size and distribution, altered fiber morphology from tubular to flat and reduced elasticity of the membrane. Airway re-opening was mimicked by introducing air bubbles over the seeded layer of A549. The endothelial layer in this system was presented by the human umbilical vein endothelial cells (HUVEC). The cellular responses in this system were measured through the distribution of actin filaments and the formation of tight junctions in epithelial and endothelial cells. The comparison of different ratios of PCL and gelatin in the nanofibrous membranes demonstrated that epithelial and endothelial cells respond differently to the mechanical properties of the membranes. Thus, A549 cells formed less tight junctions and spread more on the less dense and softer nanofibrous membranes, whereas HUVEC cells formed more actin filaments. Moreover, A549 cells showed more susceptibility to cell injury when cultured on rigid membranes [58].

Another study reported a PCL-based nanofibrous membrane that was able to support the growth of endothelial and epithelial cells for 21 days [59]. To mimic the alveolar-capillary barrier, human pulmonary endothelial cells (HPMEC) and lung epithelial cells (NCl-H441) were seeded on the membrane. To simulate inflammation during lung diseases, nanofibrous membranes were exposed to pro-inflammatory cytokines TNF-α and IL-8 to induce inflammation response through reduction of tight junction between epithelial cells that was measured by the amount of secreted intercellular adhesion molecule 1 (sICAM). The level of sICAM was higher in the apical layer compared to the basal layer. Additionally, these PCL nanofibrous membranes allowed the migration of neutrophils from the apical to the basal side of the membrane despite almost twice the smaller pore size in comparison to the 3 μm pore sizes in the control PET membranes. This demonstrates that despite smaller pore size, nanofibrous PCL membranes were able to mimic inflammatory response by allowing transmigration of neutrophils through the simulated alveolar-capillary barrier.

In general, PCL-based nanofibrous membranes demonstrated a good resemblance to the native ECM and basement membrane. The Young's Modulus of pre-wetted PCL membranes was 7.2 MPa [58] and 9.7 MPa for dry PCL membranes [59], which was close to the native alveolar basement membrane [62, 63]. Additionally, in comparison to the control PET membrane, high production of collagen on PCL nanofibrous membranes was observed [59].

A biodegradable and biocompatible PLGA polymer was solubilized in trifluoroethanol (TFE) to fabricate nanofibers for a lung-on-chip system [60]. To simulate the tumor microenvironment in alveoli, two or three types of cells were seeded: A549, fetal lung cancer cells (HFL1), and HUVEC cells. For a two-cell system, A549 was seeded on the outer side of the nanofibrous membrane, whereas HFL1 cells were seeded on the inner side of the membrane facing the microchannel. For a three-cell type system, the distribution of cells on the membrane was similar to the two-cell system, only there was a second microchannel, where the HUVEC cells were seeded on the membrane facing it (Figure 2C). Additionally, anti-cancer drug gefitinib was tested in the two-cell system. The addition of the drug leads to a significant reduction in viability of A549 cells, demonstrating the efficiency of the drug in inducing apoptosis of cancer cells. In the three-cell system, A549 cells induced apoptosis of HUVEC cells and migrated through the membrane onto the other

side. This multi-cellular microfluidic system simulated the tumor microenvironment by mimicking tumor invasion.

A simulation of the alveolar air-tissue interface was demonstrated using gelatin nanofibers [61]. Gelatin is a degradation product of collagen, which is commonly found in the basement membrane and ECM. To electrospin the nanofibers, gelatin from porcine skin was solubilized in the mixture of acetic acid, ethyl acetate, and water. Due to the high hydrolytic degradation rate of gelatin in water, the fabricated nanofibers were crosslinked with N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride and N-hydroxysuccinimide. The nanofibers were directly electrospun on a hexagonally-shaped honeycomb PDMS microframe (Figure 2D). However, SEM images demonstrated the loss of fiber integrity that resulted in a microporous structure of the membrane. A549 cells were seeded on the membrane and were supported with a culture media flow in the basal channel. An airwave was applied on the apical side of the membrane to introduce mechanical strain on the grown cell layer. The introduced mechanical strain simulating a 5% physiological strain did not affect the viability and proliferation of the cells. However, periodically applied strain reduced cell attachment to the nanofibers, which resulted in a better and more homogenous redistribution of A549 cells on the membrane.

Conclusions

The advances in micromachine fabrication led to the development of lung-on-chip models that combine anatomy, material science, and physical properties to explore the lung microstructure. Development of functional basement membrane remains challenging as existing models have drawbacks such as properties to absorb small molecules in case of PDMS or the inability to mimic mechanical parameters as in hydrogels. In comparison, electrospun nanofiber membranes might be optimized by parameters such as thickness, porosity, fiber morphology, and others. Despite being more fragile, they are gaining attention in the microfluidics area. Nanofiber-based membranes in lung-on-chip devices demonstrated good properties in cell transmigration, mimicking the disease conditions, and succeeded in its barrier function. All the studies demonstrate nanofiber membranes as a promising candidate for mimicry of basement membrane in lung tissue.

Acknowledgments

This research was funded by the Ministry of Education and Science of the Republic of Kazakhstan Grant for young scientists: AP09058308, the Nazarbayev University Faculty-development research grant: 080420FD1910 and the social policy grant awarded to Gulsim Kulsharova.

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Наноталшықты мембраналарды микрофизиологиялық жүйелерде қолдану

«Ағзадағы-чип» микрофлюидті құрылғысы дәрі-дәрмектің уыттылығын зерттеуде жануарларды сынауды алмастыра алатын перспективалы құрал болып табылады. «Өкпедегі-чип» құрылғысы бөлшектердің, газдардың және өкпе тініндегі химиялық заттардың уыттылығын бағалау үшін, сондай-ақ ауырған жағдайда дәрілердің тиімділігі мен уыттылығын зерттеу үшін қолданылады. Сонымен қатар, «өкпедегі-чип» құрылғысы денсаулықтың жағдайын, демікпе, қатерлі ісік, аутоиммунды және жұқпалы аурулар сияқты аурулардың кең ауқымын анықтауға мүмкіндік береді. Мақала микрофизиологиялық платформа шеңберінде функционалды базалды мембрана ретінде электриірілген наноталшықты мембраналарды қолдануға арналған. Мұнда микрофлюидті құрылғылар және «өкпедегі-чип» құрылғыларының тұжырымдамасы қысқаша берілген, базалды мембрананың маңыздылығы сипатталған. ПДМС, ПК сияқты қолданыстағы базалды мембрана үлгілері, гель негізіндегі мембраналар, оның ішінде оларды пайдалану барысында туындайтын қиындықтар мен кемшіліктер сипатталған. Электриірінді және наноталшықты мембраналар туралы түсініктеме берілген. «Өкпедегі-чип» құрылғысында қолданылатын наноталшықты мембраналар қарастырылған. Наноталшықты мембраналарды синтездеу үшін әртүрлі полимерлі материалдарды қолдану және мембрананы құрылғыға енгізудің әртүрлі әдістері сипатталған. Осылайша, электриірілген әдісімен алынған наноталшықты мембраналар жақсы механикалық қасиеттерді көрсетеді, иммундық жасушаларды тасымалдауға мүмкіндік береді және жасуша өміршеңдігі мен пролиферациясына әсер етпестен физиологиялық керілуді қамтамасыз етеді.

Кілт сөздер: микрофлюидтер, микрофизиологиялық, наноталшық, базалды мембрана, электроспиннинг, өкпедегі-чип, поликапролактон, жабысатын қоспа.

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Применение нановолоконных мембран в микрофизиологических системах

Микрофлюидные устройства «орган-на-чипе» — многообещающие платформы, которые потенциально могут заменить испытания на животных в исследованиях токсичности лекарств. Устройства «легкие-на-чипе» используются для оценки токсичности частиц, газов и химических веществ на ткани легких, а также для изучения эффективности и токсичности лекарств при заболеваниях. Устройства «легкие-на-чипе» позволяют имитировать здоровое состояние, а также широкий спектр заболеваний,

таких как астма, рак, аутоиммунные и инфекционные заболевания. Этот обзор посвящен использованию электропряденных нановолоконных мембран в качестве функциональной базальной мембраны в рамках микрофизиологической платформы. Здесь кратко представлена концепция микрофлюидных устройств и устройств «легкие-на-чипе», описана важность базальной мембраны. Затем изучены существующие модели базальной мембраны, такие как ПДМС, РК, мембраны на основе геля, включая проблемы и недостатки, связанные с их использованием. Затем вводится понятие электропрядения и нановолоконных мембран. Наконец, рассмотрены мембраны из нановолокна, применяемые в устройствах «легкие-на-чипе». Описано использование различных полимерных материалов для синтеза мембран из нановолокна и различные методы включения мембраны внутрь устройства. Таким образом, мембраны из нановолокна, полученные методом электропрядения, проявляют хорошие механические свойства, позволяют трансмигрирование иммунных клеток и обеспечивают физиологическое натяжение, не влияя на жизнеспособность и пролиферацию клеток.

Ключевые слова: микрофлюидика, микрофизиологический, нановолокно, базальная мембрана, электроспиннинг, легкие-на-чипе, поликапролактон, слипчивое соединение.

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