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Review

Importance of human umbilical vein endothelial cells in experimental cardiovascular studies

Deneysel kardiyovasküler çalışmalarda insan umblikal ven endotel hücrelerinin önemi

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Abstract

Nowadays, cardiovascular system disorders caused by narrowing or obstruction of the vascular system lead to the most important diseases that have a negative effect on the quality of life and have fatal consequences. It is known that many diseases are accompanied by cardiovascular system disorders. For these reasons, studies on the existence of different pathways activated in cardiovascular pathology and the investigation of these pathways have come intoquestion, and in vitro methods have been needed to be developed. in vitro cell culture models are the preferred models to enable understanding the mechanisms that regulate the process of angiogenesis. Human umbilical vein endothelial cells (HUVEC) are one of the most common in vitrocell models used in vascular studies within the scope of cardiovascular pathology. This review focuses on the use of HUVECs as an in vitro model to evaluate different therapeutic approaches.

Keywords: human umbilical vein endothelial cells; cardiovascular diseases; in vitro; models

Öz

Günümüzde damarlarda daralma veya tıkanma sonucunda ortaya çıkan kardiyovasküler system bozuklukları, insanların yaşam kalitesini olumsuz yönde etkileyen ve ölüm ile sonuçlanabilen önemli hastalıkların başında gelmektedir. Bilinen birçok hastalığa kardiyovasküler system bozuklukları eşlik etmektedir. Bu nedenlerle kardiyovasküler patolojide active olan farklı yolakların varlığı ve bu yolakların incelenmesine yönelik çalışmalar gündeme gelmiş, in vitro metodların geliştirilmesine ihtiyaç duyulmuştur. In vitro hücre kültürü modelleri, anjiyogenez sürecini düzenleyen mekanizmaları anlamamızı sağlamak için tercih edilen önemli modellerdir. İnsan göbek ven endotel hücreleri (HUVEC), kardiyovasküler system patolojileri ile ilgili çalışmalarda kullanılan en yaygın in vitro hücre modellerinden biridir. Bu derlemede, farklı terapi yaklaşımlarının değerlendirilmesi için HUVEC'lerin in vitrobir model olarak kullanım alanları üzerinde durulmuştur.

Anahtar Kelimeler: insan umblikal ven endotel hücresi; kardiyovasküler hastalıklar; in vitro; model

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Introduction

The lumen in human blood vessels is covered with a very thin endothelial cell (EC) layer.HUVECs become one of the most common types of vascular ECs for angiogenesis studies. These cellsplay a crucial role as a modelplatform for the study of the organization of ECs function and the investigation of atherosclerotic plaques and angiogenesis as a result of the reaction of the blood vessel wall of the endothelium to shear stress [1].

Angiogenesis; play a role in the pathophysiology of many different diseases like atherosclerosis, rheumatoid arthritis, tumor growth, anddiabetic retinopathy. It also plays a therapeutic role in the response to hypoxia in vascular structural disorders. Angiogenesis consists of three stages, which involve the proliferation, migration and remodeling of endothelial cells in the process of etiology.

HUVECs obtained by primary isolation are the most popular ECs used in cardiovascular research because human umbilical vessels are more common than other blood vessels. HUVECs can be isolated and protected by the standard protocol with a relatively minimal requirement [2,3] orpurchased from commercial resources (e.g. American Type Culture Collection -ATCC).The perfusion method of the human umbilical cord vein with collagenase is used to obtain asingle-layer of endothelial cells that line this vessel[4].At the early stages of passages of these cells, which are grown in the presence of heparin, maintain almost all of the properties of native vascular endothelial cells.Briefly these features are growth factors, cytokines, vasoactive ligands, vascular endothelial growth factor (VEGF), and fibroblast growth factor (FGF). In addition to these features, they may also express the endothelial cell-specific markers such as von Willebrand factor and an endothelial specific adhesion molecule (CD31), tumor necrosis factor (TNF-α) and angiotensin II[5].HUVECs also express many crucial endothelial markers, e.g. intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1) and selectins,as well as signaling molecules associated with vascular physiologysuch as NO [6].Under specific conditions, HUVECs could be used as an improved model by differentiating to 3D spheroid cultures [7] or 3D co-cultures [8]to better understand the in vivo behavior of ECs.There are also studies showing that HUVECs respond to physiological and/or pathological stimuli such as high glucose, lipopolysaccharide (LPS) and shear stress[9-11].HUVECs have therefore been accepted as a general model for ECs in both normal and diseased conditions, although human umbilical vessels are only at certain stages of human life. Therefore, in addition to cells obtained with primary isolation, immortalized endothelial cell lines have been developed. For this purpose, the permanent cell lines and HUVECs are combined by fusion to obtain infinite proliferation properties.

HUVECs provide an important in vitro model environment to obtain evidence of cellular and molecular events in the pathophysiology of atherosclerosis and plaque formation. It has also been used as a model to describe angiogenesis or neovascularization in response to hypoxia or ischemic tissues [12].

HUVECs are also used as a single-layer cell platform to assess the association of white blood cells (eg, leukocytes, macrophages) with the endothelial cell layer in vascular tissues to investigate the potential behavior of kinases, chemokines, andadhesion molecules [13].HUVECs are designed as monolayers on amorphous surfaces or sections to monitor the effects of blood flow on endothelial cell function in vivo.These monolayer cells have been used to identify transcription factors such as KLF2, which regulate the expression of adhesion molecules such as vascular cell adhesion molecule-1 and endothelial adhesion molecule E-selectin in response to pro-inflammatory cytokines such as cell adhesion TNF-α which plays a role in the early stages of atherosclerosis [14,15].

In the light of this information's, it is necessary to identify cell culture systems that simulate the damaged tissue physiology in vivo.This review aims to highlight the status of the use of HUVECs as an in vitro model for the evaluation of many different therapy approaches.

In vitro usage of HUVECs

In a recentresearch report, HUVECs have been proposed as amainin vitro model for all angiogenesis-forming steps. In this study, HUVEC culture in Matrigel, a basement membrane matrix, has been shown toinduce the formation of honeycomb structures that simulatingin vivotube formation process of endothelial cells[16]. By investigating the effects of transforming growth factor-β, VEGF, hypoxia, FGF, and angiogenesis inhibitors on the composition and organization of honeycombs produced by HUVECs has been revealed these factors role in both pathological and therapeutic angiogenesis.

In another study,in vitrouses of HUVECs have been described as a major role in angiogenic activityof notoginsenoside R1 (R1), a mainsaponin found in Panaxnotoginseng. In this study, they showedthat R1 stimulates and markedly enhanced proliferation oftube formation ability of HUVECs [17].

Another area forusing the in vitro model of HUVECs is the field of cardiovascular tissue engineering. In a study conducted, HUVECs defined as a promising source of cells because of their excellent growth characteristics for cardiovascular tissue engineering and their phenotypes similar to those in the native tissue [18].

Endothelial cells are known to have an important role in many

physiological and pathological processes of the cardiovascular system. Especially from the surface proteoglycans of these cells; syndecan-4 plays an important role in such processes. Thus, syndecan-4 is known to play a role in controlling the release of different factors from endothelial cells and the presence of these factors near endothelial cells and their environment. In light of this information, significant changes in CXCL8 secretion observed after Syndecan-4 knockout have been shown to affect the autocrine regulation of angiogenesis. In addition, Syndecan-4 silencing has been reported to cause changes in cellular morphology and to cause delayed capacity of HUVEC wound closure and tube formation [19].

Conclusion

It has been emphasized that the widespread use of HUVECs can be considered as a relatively reliable and simple in vitro model for ECs and that more studies should be done by focusing on this subject. At the same time, it has been shown that future studies on angiogenesis are expected to be used to predict and understand the biological responses of ECs with in vitro models of HUVECs.

Declaration of conflict of interest

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