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Editorial Open Access

Human Endothelial Progenitor Cell Application in Vascular Diseases Seen in Metabolic Syndrome

U. Deniz Dincer*

Department Chair of Basic and Clinical Pharmacology, Bezmialem Vakif University (BAVU) School of Medicine, Turkey

***Corresponding author:** Dr. **U. Deniz Dincer**, Department Chair of Basic and Clinical Pharmacology, Bezmialem Vakif University (BAVU) School of Medicine, Turkey, Tel: 539 811 9829; E-mail: UDincer@bezmialem.edu.tr

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Editorial

Intact endothelial cells and their progenitors receive, integrate and response to physiological and pathological environment and play an important role in cardiovascular disease development and angiogenesis. When Furchgott et al. demonstrated that a healthy intact endothelium is necessary to continuation of vascular function, it truly revealed a different point of view [1]. The new era, vascular adaptation requires intact healthy endothelial cells to response physiological and pathological environment, displayed different therapeutic approaches in cardiovascular diseases. Generation of more information such as endothelial cells release a short-lived vasodilator agent which called nitric oxide via eNOS also was shook down the previous approaches in vascular disease management [1]. Furthermore, Asahara et al. were isolated endothelial progenitors from human peripheral blood in 1997 and they clearly demonstrated that those progenitors are actually differentiated into endothelial cells in adults [2]. It was completely started to predominant paradigm in previous treatment modalities regarding a new vessel formation probable via their progenitors in adults after embryonic development [2]. Because, until that time it was believed that endothelial differentiation could only occur during embryonic development [2]. Thus, endothelial progenitors are important as intact endothelial cells and the information "during different physiological and pathological stress a larger amount of endothelial progenitors released and mobilized into the peripheral blood furthermore display vasodilatation and generate a new vessel formation to re-establish blood flow" is impressive as intact endothelium necessary to vessel function knowledge.

Metabolic syndrome is characterized by a combination of obesity, hypertension, insulin resistance, dyslipidemia, impaired glucose tolerance furthermore significantly elevated cardiovascular morbidity and mortality [3]. One of the main and frequent complications seen is cardiovascular disease such as coronary and peripheral arterial disease as well as myocardial infarction which could be related with decreased endothelial progenitor cell adaptation. Stroke incidence was also found increased in metabolic syndrome. Thus, new treatment modalities related vascular management is important to metabolic syndrome which has together with cardiovascular complications.

Some of the brand new strategies are aiming to inject high proliferative blood vessel forming endothelial progenitor cells which convertible to human pluripotent stem cells to the ischemic or injured vascular sites [4]. Adult peripheral and cord blood contain endothelial progenitor cells which represent a minor subpopulation of blood mononuclear cells [5,6]. Isolated endothelial cells also contain different subpopulations such as colony-forming unit endothelial cells (CFU-ECs) and endothelial colony-forming cells (ECFCs) [5,6]. Decrease in CFU-EC colonies is oppositely correlated with vascular disease however, ECFCs associated with angiogenesis and apoptosis furthermore ECFCs functional capacity related with de novo vessel formation and coordinate vessel forming ability including cell survival, proliferation, migration, and capillary-like structure formation of endothelial cells [5]. Human umbilical cord blood (HUCB) ECFCs truly consider human pluripotent stem cells (hPSCs), also called blood outgrowth endothelial cells which display highly respectable vessel regeneration potential and new vessel forming ability [4]. Thus, ECFCs could replace with injured ischemic vascular cells and able to normalize blood flow [4]. Similar treatment approach could implement to many more diseases such as stroke, cardiovascular disease, limb injury, ischemic ophthalmic and hypoxic pulmonary artery diseases. Indeed, some of the latest research was focused on to rise a cell as same as HUCB ECFCs from any other human cells. Previous investigations were revealed that when transplanting those cells into the ischemic or infarcted lesion in the heart, brain, eye, lung or injured limb area they actually able to improve blood flow even further generate a new vessel formation [4].

Although the ECFCs actively usage in the clinics mandatory was limited because of implanted endothelial progenitor cell survival duration and function however, the expectations were getting a rise. New results related hPSCs were significantly promoted to test their regeneration capacity in tissue ischemia, vascular injury and trauma. Demonstration of their incorporation to injured artery and functional response of implanted progenitor cells to neuro humoral stimulus were encouraged to develop ongoing further investigations [4-6]. Some of the new researches were focused on to examine best conditions for implantable endothelial progenitors which they actively incorporate injured endothelial sites and generate a new vessel formation. The other important research topic was to understand underline mechanisms of hypoxia induced development of endothelial progenitor cell apoptosis. A larger amount of EPCs are released and mobilized into the peripheral blood to constitute vasodilatation and increase vessel formation by hypoxia. Generally chronic hypoxia displays apoptosis-mediated cell death instead of the generation of new vessel formation and endothelial repair (Figures 1 and 2). Consequently, the duration of hypoxia is the key moderators to generate re-endothelialize injured vessels and re-establish blood flow via new vessel formation as well as vasodilatation (Figure 2) or to generate apoptosis via exhibits cell death (Figure 1). Interestingly, ECFCs which obtained from HUCB express endothelial, angiogenic and hypoxic markers such as VE-cadherin (vascular endothelial-cadherin, CDH5, CD144), endothelial nitric oxide synthase (eNOS), endothelial cell adhesion molecule (PECAM; CD 31), vascular endothelial growth factor A (VEGFA), insulin-like growth factor 1 (IGF-1), adrenomedullin (ADM), G protein coupled activity modifying protein 2 (RAMP 2) [7].

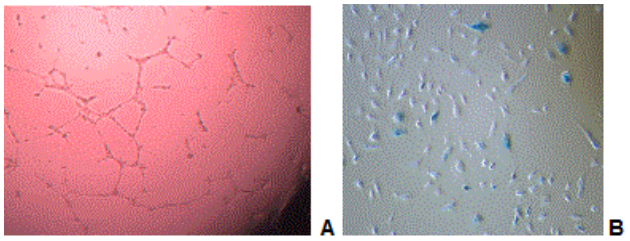

Figure 1: A. Matrigel Assay; Photomicrograph represents tube formation; vessel forming capacity of human umbilical cord blood (HUCB) derived endothelial progenitors (ECFCs) applied with in vitro 7 days hypoxia B. Senescence Assay, Photomicrograph represents clonogenic capacity of cells; which increasingly stained positively with SA β-Gal of HUCB ECFCs.

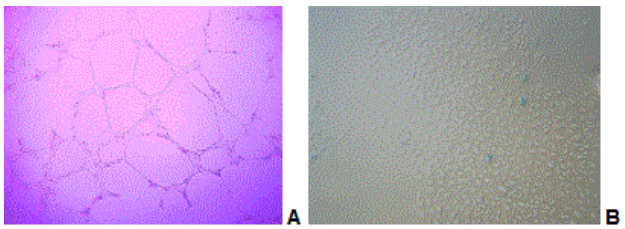

Figure 2: A. Matrigel Assay; Photomicrograph represents tube formation; vessel forming capacity of human umbilical cord blood (HUCB) derived endothelial progenitors (ECFCs) applied with regular cell culture medium B. Senescence Assay, Photomicrograph represents clonogenic capacity of cells; which normally stained positively with SA β-Gal of HUCB ECFCs.

Endothelial progenitor cells are critical regulators of new vessel formation and angiogenesis which able to initiate re-vascularization, vascular repair and new vessel formation to straighten vascular function. Endothelial repair and growth linked with the incidence of development of hypoxic vascular diseases such as cardiovascular disease which generates in metabolic syndrome. Thus, the new era could be using high clonal proliferative potential human pluripotent stem cells (hPSCs) such as HUCB ECFCs to normalize vessel function via their self-repopulating capacity and vessel forming ability during ischemic conditions. It could generate different treatment approaches in cardiovascular complications seen in metabolic syndrome.

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