

*Editorial***ENDOTHELIAL PROGENITOR CELLS – ROLE IN ATHEROGENESIS***Simona Georgiana Popa* , *Maria Mota*Department of Diabetes, Nutrition and Metabolic Diseases,  
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Atherosclerosis is the most important arterial disease worldwide and the leading cause of cardiovascular diseases. Endothelial dysfunction induced by various cardiovascular risk factors represents a pivotal step in initiation and progression of atherosclerotic vascular diseases.

Endothelial progenitor cells (EPC) represent an important step in endothelial cell regeneration through direct engraftment and indirect release of angiogenic factors, thus contributing to improving endothelial dysfunction [1]. EPC physiology and the factors that modulate their number and activity are incompletely elucidated.

EPC are a heterogeneous bone marrow-derived cell population which share common properties and functions and which co-express hematopoietic (CD34, CD133) and endothelial markers such as CD31, VEGF receptor-2 (VEGFR2, KDR), vascular endothelial cadherin, endothelial nitric oxide synthase (eNOS). The evaluation of EPC is represented by flow cytometry using three antigens based (CD34, KDR and CD133) protocol [2]. In culture, EPC have the ability to proliferate, to form colony, to migrate, to adhere at mature endothelial monolayer and to

incorporate into vascular networks on matrigel [3-5]. According to the EPC time-dependent appearance in culture were identified two type of EPC: early and late EPC. Early EPC appear in culture after 4-7 days from seeding of mononuclear cells and express endothelial and hematopoietic surface markers, but possess only low angiogenic capacity [6-8]. Late EPC appear at 3-4 weeks after primary seeding, mostly express endothelial surface markers and possess the ability to form functional vessels [9-10].

Taking into consideration the difference between early and late EPC regarding the function and expression of surface antigen it is possible to be other differences related to EPC differentiation or EPC involvement in atherosclerosis regression. Therefore, it is more likely that early EPC to be monocyte/macrophage cells progeny and to promote cholesterol efflux, whereas late EPC to be endothelial cells progeny.

The EPC numbers and functions are compromised in subjects with atherosclerotic risk factors such as dyslipidemia, diabetes, hypertension, obesity [11-13].

Numerous studies indicated that subjects with diabetes mellitus have decreased number

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of EPC, impaired EPC function, decreased nitric oxide availability and increased ROS production comparative with healthy subjects [13-14]. Felice *et al* demonstrated that EPC have resistance to oxidative stress induced by high glucose exposure due to increased activity of glutathione peroxidase [15].

Several lines of evidence indicate that human HDL can increase circulating EPC number, stimulate EPC differentiation, ameliorate EPC function, increase nitric oxide availability and decrease EPC senescence and ROS production [11-12,16], but the underlying mechanisms are incompletely understood.

The level of oxidized low-density lipoprotein (OxLDL) increases in subjects with cardiovascular ischemic disease, diabetes or dyslipidemia and serves as an independent predictor for future cardiac events in these patients [17-18]. Previous studies indicated that OxLDL increased EPC senescence and impaired its functions by binding to lectin-like oxidized low density lipoprotein receptor (LOX-1) from EPC surface [19-20].

It is of interest to know whether EPC expression of LOX-1 is involved in the effects of OxLDL on the cholesterol efflux from EPC to HDL depending on the presence of diabetes, low cholesterol or clinical atherosclerosis.

Various studies have demonstrated the important role of EPC in vasculogenesis and angiogenesis of ischemic tissue but only a few studies have concentrated on the role of EPC in atherosclerosis. Conflicting data have been provided regarding the effect of EPC on plaque progression and phenotype.

Recent studies indicated that EPC exert an anti-atherosclerotic effect under physiologic condition but they may, also, contribute to

plaque progression and instability in advanced atherosclerotic plaque under specific pathological condition [8].

Several studies demonstrated the therapeutic potential of EPC transplantation in animal models with hindlimb ischemia, but also in patients with acute myocardial infarction [21-23]. Ma *et al* showed that EPC inhibits atherosclerosis progression in rabbit models with atherosclerosis induced by high cholesterol diet and balloon injury [24]. Accumulating evidence indicates that implantation of EPC-capture stents was successfully in terms of low incidences of repeat revascularisation and stent thrombosis in patients with coronary heart diseases [25].

Contrary, other study demonstrated that in patients treated with EPC-capture coronary stents were frequently observed clinically-justified target lesion revascularization and binary restenosis [26].

Some evidence shows that transfer of spleen-derived EPC and bone marrow cells increased atherosclerosis lesion size, induced change in the plaque composition (smaller fibrous caps and larger lipid core) and increased oxidative stress in the ApoE KO mice [27]. The injected EPC and bone marrow cells were found predominantly within the lipid core of the atherosclerotic plaque and not in the endothelial or subendothelial areas [27].

In spite of the potential influence of proatherogenic factors on circulating EPC level, phenotype and function, these variables remains poorly explored.

EPC may play an important role in atherosclerosis and this would allow defining the best molecular targets for drug development to stop atherosclerosis or even to induce atherosclerosis regression.

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