PHENOTYPIC OVERLAP BETWEEN MONOCYTES
AND VASCULAR ENDOTHELIAL CELLS

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1. SUMMARY

During embryonic development, endothelial cells (ECs) develop organ specific properties. ECs express specific markers, which are helpful in identifying these cells in vivo and in culture. Interestingly, most of the supposed specific endothelial markers are present on both ECs and hematopoietic precursors or mature blood cells, which correspond to the idea of a common embryonic precursor. Monocytes/makrophages and monocyte-derived dendritic cells, as more differentiated hematopoietic cell populations, show a wide phenotypic overlap with particularly hepatic sinusoidal, and microvascular endothelial cells within inflamed tissue, such as neovascularised complicated atherosclerotic plaques. Furthermore, under local angiogenic growth conditions monocytes or monocyte precursors or immature dendritic cells may differentiate into endothelial like cells. First evidence suggests an endothelium-independent revascularization potential carried by monocyte-derived macrophages. These macrophages have been shown to form tunnel-like structures in ischemic regions. Future studies have to address the question, whether monocyte-/dendritic cell-derived endothelial like cells can develop a similar functional behaviour in vasoregulation, coagulation and fibrinolysis, as described for vascular endothelial cells, and thus may contribute to neoangiogenesis by a direct vessel-forming role.

2. INTRODUCTION

During embryonic development, endothelial cells develop organ specific properties. The acquisition and maintenance of specialized properties by endothelial cells is important in the functional homeostasis of the different organs. ECs express specific

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Novel Angiogenic Mechanisms: Role of Circulating Progenitor Endothelial Cells.
ENDOTHELIAL CELL MARKER

**Endothelial Constitutive Markers**

- vWF
- CD31/PECAM
- ACE
- Type I LDL receptor
- Ulex europaeus
- VE-cadherin
- CD105
- CD36
- Thrombomodulin

**Inducible Endothelial Markers**

- CD54/ICAM-1
- CD106/VCAM-1
- CD62E/E-selectin
- CD62P/P-selectin
- Flk-1/KDR
- Flt-1
- Tie-1
- Tie-2/Tek

Figure 1. Examples for constitutive and inducible endothelial cell markers which are helpful in identifying these cells in vivo and in culture (e.g. von Willebrand factor, VE-cadherin, Ulex europaeus, CD105). Some of the EC markers are constitutive and present in essentially all types of endothelium. Other molecules are expressed only after activation by inflammatory cytokines or growth factors. (Figure 1.) Some markers are rather specific for EC of different origins, such as from the brain and blood brain barrier (BBB) or bone marrow or the lymphatic system. This last category is relatively scarce, because EC isolation from the microvasculature of certain vascular regions is still technically difficult, and once in culture, they tend to lose their specialized properties (references in 1). Only in the past few years the technology has become available which permits the in situ study of ECs. New techniques are under development such as the injection of phage-display peptide libraries, which detect specific surface molecules in the peripheral endothelium in vivo.

Interestingly, most of the supposed specific endothelial markers are present on both ECs and hematopoietic precursors or mature blood cells, which correspond to the idea of a common embryonic precursor. Recently, several lines of evidence suggest the existence of circulating endothelial precursor cells in adult organisms. In summary these data indicate, that only a very small subset of circulating hematopoietic (stem?) cells expressing the surface markers AC133 and/or AC133/Flk-1/CD34, have the capacity to differentiate into endothelial cells. This indicates that these cells represent...