THE ENDOTHELIAL CELL

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The "endothelium" was a controversial subject in the 80s due to its unclear definition. Considering the differences between species, the endothelium may refer to the simple squamous epithelium that lines the vascular lumen in vertebrates but it may also represent any cell type that comes into contact with the vascular lumen (Munoz-Chapuli et al, 2005). A number of debates regarding the origin of the endothelial cell emerged between the years 1997 and 2003.

The classical hypothesis supports the existence of a common precursor for endothelial cells and erythrocytes known as the hemangioblast, while the more recent hypotheses support the origin of the endothelial cell from a common vascular progenito derived from stem cells (Munoz-Chapuli et al, 2005). Currently, the origin of the endothelial cell is strongly linked to vasculogenesis, a process through which vessels are formed directly from mesenchymal cells. According to these aspects, endothelial cells appear in both the extra-embryonic mesenchyma and in the embryo, from precursor cells known as angioblasts. Endothelial cells are directly implicated in angiogenesis and lymphangiogenesis and a series of pro-angiogenic (eg. VEGF, PDGF) and anti-angiogenic (Angiostatin, Endostatin) factors exert their effects on them (Jitariu et al, 2015). These factors are maintained in a permanent equilibrium in normal conditions. Angiogenesis cannot be separated from lymphangiogenesis and in order for the two processes to occur, the presence of a series of signaling molecules, such as VEGF and PDGF (Ferrara et al, 2009; Raica et al, 2010), and a normal/typical blood/lymphatic vascular structure are needed.

The endothelium is found in blood and lymphatic vessels and in the structure of the endocardium. Lymphatic endothelial cells are immunophenotypically different from the endothelial cells of blood vessels (Adams et al, 2007). Due to this reason the terms ECs and LECs are used in order to distinguish endothelial cells that line the lumen of blood vessels from those that line the lumen of lymphatic vessels (Petrova et al, 2002). In optical microscopy, the endothelial cell has a flattened morphology, with irregular cell borders, an oval nucleus without visible nucleoli but with large blocks of chromatin. Electron microscopy analysis reveals the presence of non-specific (microtubules, microfilaments) and specific organelles, the Weibel-Palade corpuscles, with an elongated shape and an internal tubular structure.

Before the discovery of the lymphatic endothelial cell markers, a number of errors occurred during blood vessel counting, their number being overestimated. Blood vessel endothelial cell markers such as CD31 and CD34 were also positive for the lymphatic endothelium. The discovery of the immunohistochemical spectrum of the lymphatic endothelium (eg. Prox-1, Lyve-1, podoplanin) has large benefits (Cao et al, 2004) for the proper estimation of the microvessel density (MVD) and of the lymphatic microvessel density (LMVD).

The implications of endothelial cells in human pathology are not limited to tumor angio- and lymphangiogenesis but also refer to benign and malignant vascular tumors derived from endothelial cells. The most frequent benign vascular tumors in medical practice are hemangiomas and lymphangiomas exhibiting different histopathological variants as well as hemangioendotheliomas (Kumar et al, 2013), associated with a high risk of post-excisional recurrence. The most common malignant vascular tumors are angiosarcomas, lymphangiosarcomas and Kaposi sarcoma (Kumar et al, 2013). Out of these, lymphangiosarcomas are extremely controversial entities due to their unclear nature. Currently it is not well established whether lymphangiosarcomas are true malignant tumors or if they represent vascular obstructions through lymphatic permeation.

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