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Endothelin-1 release from endothelial cells from blood vessels compared with those derived from stem cell sources

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Stem cell-derived endothelial cells are being investigated as research tools and cell therapy for vascular disease. A number of sources of stem cell derived cells exist. These include human embryonic stem cell-derived endothelial cells (hESC-EC) and bone marrow derived progenitor cells that can be expanded to give blood outgrowth endothelial cells (BOEC). Endothelial cells release key hormones that define their phenotype and mediate cardiovascular health and disease. The potent vasoconstrictor hormone endothelin (ET-1) is a key endothelial hormone, elevated levels of which are associated with vascular inflammation. The full extent of how stem cell derived endothelial cells function is not known, particularly in terms of release of vasoactive hormones. In the current pilot study we have compared the ability of two types of endothelial cells from mature vessels, namely human umbilical vein endothelial cells (HUVECs) and human lung microvasculature endothelial cells of the lung (HMVEC) with two types of 'stem cell' endothelial cells, namely, hESC-EC and BOEC to release ET-1. ET-1 is produced by endothelial cells under basal culture conditions, but can be increased further by agonists including thrombin. In the current study we have investigated release under 'basal' culture conditions. hESC-EC[1] and BOEC[2] were derived as described previously. All cells were cultured for 24h in endothelial cell specific medium (Promocell-MV2). ET-1 release in conditioned media was measured by ELISA. HUVEC, HMVEC and BOEC released relatively high levels of ET-1 (>50 pg/ml), consistent with an 'endothelial cell phenotype'. By contrast, hESC-EC released undetectable levels of ET-1. As ET-1 can contribute to cardiovascular disease this could represent a benefit of hESC-EC, over BOEC in the repair and regeneration of the endothelium of a damaged organ. These findings will be important to follow up with cells of a range of donors and may be important in the future optimal use of stem cell derived endothelial cells in human disease.

1 Földes, G. et al. (2010) PLoS One. **5**, e10501
2 Ingram, D. A. et al. (2004) Blood. **104**, 2752-2760.

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