Alteration of the Essential Role of Endothelial Cells for Promoting Self-Renewal and Lineage Differentiation by Glucosylceramide and 16,16-dimethyl Prostaglandin E2

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Bone marrow endothelial cells (BMECs) play an essential role for supporting hematopoietic stem cell expansion, self-renewal, and lineage differentiation. It has been known that BMECs receiving chronic constitutive inflammatory signals play a significant role in promoting functional alterations in hematopoietic stem cells (HSCs). Among many types of Inflammatory agents, bioactive lipids, including glucosylceramide (GlcCer) and dimethyl-Prostaglandin (dmPGE2) has been recently shown to be the potent mediator of inflammation through their own cognate receptor, CLEC4E (Mincle) and PGE receptors, respectively. Despite their biological significance, however, it is not known if GlcCer and dmPGE2, directly induce gene expression of self-renewal and lineage differentiation factors in BMECs or any other endothelial cells in general. We attempt to model the effect of GlcCer and dmPGE2 *in vitro* by employing primary human vein endothelial cells (HUVECs), and modified HUVECs transduced with E4ORF1 enhancing glucose uptake pathway. We hypothesize that GlcCer and dmPGE2 treatment will trigger reduction in the expression of ANGPTL2, JAG1, and PTN, while an increase in KITLG, CCL5, M-CSF, and GM-CSF in HUVEC. The significance of this study could be identifying a major pathway that contributes to the loss of self-renewal and increased myeloid lineage differentiated mediated by endothelial cells upon exposure to GlcCer. Results showed varied expressions of self-renewal and maintenance genes by GlcCer and dmPGE2. In conclusion, HUVEC may not be a good model for *in vitro* study as there was no expression seen in the lineage differentiation gene M-CSF and varied GM-CSF expression. However, the results of our study could potentially be utilized for *in vitro* expansion of HSCs for autologous bone marrow transfer, further genetic manipulation of endothelial cells, and characterization of the signal transduction pathway.