Title:	Investigating Tie2 Endocytosis
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Abstract:	TEK (Tunica Interna Endothelial cell Kinase) or Tie2 receptor is a cell surface tyrosine kinase receptor expressed almost exclusively in endothelial cells, where it is mainly studied for its role in angiogenesis. Angiopoietins, the natural ligands of Tie2, modulate Tie2-dependent signalling, which regulates endothelial cells' survival and apoptosis, controls vascular permeability, and regulates the capillary remodelling that occurs during normal angiogenesis. Tie2 has been related to various pathologies with vascular implications, such as pulmonary hypertension, diabetic retinopathy and tumour growth. The regulation of Tie2 activation and function is complex, involving multiple factors that are still under investigation. For instance, after activation by the agonistic ligand Angiopoietin-1 (ANGPT1), Tie2 is internalised in cells by an endocytic mechanism that has yet to be explored. It has been observed that endocytosis of molecules can be involved in a regulatory role in intracellular signalling in various ways. I believe that the endocytosis of Tie2 may also be essential in the regulation of its activity and cellular output. Therefore, my master's thesis project is to investigate the domain of Tie2 and prospective proteins responsible for the endocytic mechanisms involved in the internalisation of Tie2. To facilitate the study of Tie2, I have produced different retroviruses using various prospective deletion constructs in plasmids, along with appropriate tags, in 293-GPG cells. These viruses are transfected into Human Umbilical Vein Endothelial Cells (HUVEC) to study their role in Tie2 endocytosis. I have stimulated HUVEC cells using different ligands and observed the differences in Tie2 endocytosis and its subcellular localization. I employed an immunofluorescence-based assay to confirm the internalisation and quantify the amount of internalised Tie2. Additionally, I used inhibitors of endocytosis to analyse the characteristics of Tie2 internalisation.. Furthermore, I performed gene silencing using shRNA against DNM2 which is responsible for producing Dynamin 2 protein. These results will shed light on the potential protein candidates that interact with the Tie2 receptor, contributing to its endocytosis as well as the new cellular signalling mechanisms involved in the vasculature.
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