



Category: Miscellaneous

Role of Dynamic GPCR Signaling During Germinal Matrix Blood Vessel Development

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Abstract

During brain development, blood vessels create a complex network to meet the metabolic demands of neural cells. While G-protein coupled receptor (GPCR) signaling is known to be critical in numerous physiological processes throughout the body, their role in neurovascular signaling is unclear. Our lab has found that in neural progenitors (NPCs) of the germinal matrix (GM), the GPCR S1P receptor 1 (S1PR1) activates endothelial TGF β signaling through transcriptional regulation of the TGF β activator, integrin β 8. Using chemogenetics, we are investigating the significance of temporal dynamics of this pathway in GM blood vessel maturation. By activating the GPCR pathway through Designer Receptors Activated by Designer Drugs (DREADD) we will first determine the effects of varying doses of the DREADD activator, CNO, on integrin β 8 gene expression and pathway activity using cultured primary NPCs. Then we will activate the DREADDs at specific embryonic stages to examine its effects on vessel growth, maturation, and integrity *in vivo*. These results will likely demonstrate the critical role of dynamic GPCR signaling in NPCs for proper GM vessel development. Similar experiments in a mouse model of Intraventricular Hemorrhage (IVH), a human disease prevalent in premature infants, may also provide clinically relevant information for phenotypic rescue and medical intervention.

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