# Can Clusterin Target Mutant Human GNAQ in Sturge-Weber Syndrome to Alleviate Ocular Hypertension?

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**Background/Objective:** Sturge Weber Syndrome (SWS) results from a somatic mosaic mutation of GNAQ, which encodes the alpha subunit of $G_{aq}$. This R183Q mutation disables the G-protein from exchanging ATP for ADP, restricting the receptor to its active conformation. Chronic activation results in angiomas, or benign vascular overgrowths, in the leptomeningeal, cutaneous facial, and orbital regions. Patients with SWS therefore commonly present with a characteristic port wine birthmark, focal seizures, developmental delay, and glaucoma. Management of glaucoma is particularly difficult, as SWS patients are often resistant to traditional medications and surgeries are complicated by the risk of angioma rupture. It is predicted that similar mechanisms may relieve ocular hypertension in patients with SWS. We investigated the role of the $GNAQ^{R183Q}$ in glaucoma pathogenesis and potential downregulatory molecular interventions using clusterin.

**Materials/Methods:** Analyzed data of the protein profile from total and ECM enriched fraction. To generate adenovirus human GNAQ, we received mutant and wild-type human GNAQ from Dr. Doug Marchuk, Duke University, which were cloned into Adeno-X adenoviral plasmids and replicated in Stellar competent *E. coli*. Isolated plasmids were linearized via PacI digestion and transfected into HEK-293 cells for amplification.

**Results:** In the proteomics data, we found a significant decrease in AdCLU lowered G-proteins including GNAQ, GNB1, and GNG12, and Ras-related RRAS2. The downregulation of wild-type GNAQ expression by chaperone protein clusterin as well as pharmacological inhibitors of GNAQ leading to decreased intraocular pressure. In the process of cloning the mutant adenovirus, we have the virus which will be transduced in trabecular meshwork and tested for the effectiveness of clusterin to lower the mutant GNAQ.

**Potential Impact:** This GNAQ adenovirus developed will allow to mimic the underlying pathophysiology of SWS in human and mouse tissues ex vivo and in vivo. The expression of these genes/proteins will be used for investigation into potential pharmaceutical interventions aiming to noninvasively preserve these patients' vision.