REGULATION OF CDK7 ACTIVITY THROUGH A PI (3)-KINASE/ PKC-ι MEDIATED CELL PROLIFERATION CASCADE. **Shraddha Desai, Prajit Pillai, Rekha Patel, Mildred Acevedo-Duncan.** Department of chemistry, University of South Florida, 4202 E. Fowler Ave CHE205, Tampa, FL 33620.

The main objective was to study the potential function of PKC-ι in cell cycle progression and proliferation in glioblastoma. PKC-ι is highly over expressed in human glioma and benign and malignant meningioma however little is understood about its role in glioma cell proliferation. Several upstream molecular aberrations and/or loss of PTEN have been implicated to constitutively activate PI (3)-kinase pathway. PKC-ι is one of the important downstream mediators, often upregulated by PI (3)-kinase. Results showed that PKC-ι directly associated and phosphorylated Cdk7 at Thr-170 in a cell cycle dependent manner, phosphorylating its downstream target, cdk2 at Thr-160. Cdk2 has a major role in inducing G1-S phase progression of cells. Purified PKC-ι also phosphorylated endogenous as well as exogenous Cdk7. Inhibition of PKC-ι activity by PI (3)-kinase inhibitors, PDK1 and PKC-ι siRNA reduced phosphorylation of Cdk7 and subsequently cdk2. These findings suggest presence of a novel PI (3)-kinase/PKC-ι/Cdk7/cdk2 cell proliferation pathway.