

## TITLE

### DIFFERENTIAL REGULATION OF HIF-1 $\alpha$ UNDER NORMOXIC AND HYPOXIC CONDITIONS

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L-Oxalyl diaminopropionic acid (L-ODAP), a non NMDA receptor agonist, induces the stabilization and nuclear translocation of HIF-1 $\alpha$  with maximum nuclear levels at 4 hours in chick brain. The stabilization and nuclear translocation of HIF-1 $\alpha$  was initiated at 2 hrs maximal by 4 hrs. Transiently transfected SK-N-MC human neuroblastoma cells with GFP-HIF1 $\alpha$  when treated with L-ODAP, but not D-ODAP resulted in nuclear translocation of HIF-1 $\alpha$  under normoxic conditions. Inhibition of PKC by staurosporine inhibited GFP-HIF-1 $\alpha$  nuclear translocation indicating a role of PKC in HIF stabilization. NOS and tyrosine hydroxylase expression were elevated in L-ODAP treated chick brain in a time dependent manner with maximal effect at 2 hrs post injection. Further PEBP (phosphatidylethanolamine binding protein) also down regulated in the presence of ODAP indicating stabilization of Hypoxia. While PEBP levels were not affected in the presence of desferroximine and CoCl<sub>2</sub> indicating that HIF is regulated by different signaling pathways in normoxia and hypoxia. Thus, the present study opens a new field to explore down stream signaling events associated with HIF stabilization such as VEGF and angiogenesis.