



**Title: Coenzyme Q10 Induces Apoptosis in Human Retinoblastoma Cells by Downregulating Vascular Endothelial Growth Factor**

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**Abstract:**

Retinoblastoma is a rare form of ocular malignancy in children involving uncontrolled growth of the retinal cells due to mutation in the tumor suppressor, Rb gene. The survival of children suffering from retinoblastoma is due to chemotherapy, transpupillary thermotherapy, photocoagulation, radiotherapy, orbital exenteration or even enucleation of the eye globe when the development of the tumor reaches the stage that obstructs vision. In order to escape the deadly side effects of chemotherapy in a highly conserved organ like eye present therapeutics aim to find out better options of ocular drug delivery to control retinoblastoma. Cancer signalling pathways and tumor sustenance requires the presence of reactive oxygen species (ROS) and targeting ROS has helped in the development of anticancer therapeutics. The cytotoxic efficacy of coenzyme Q10 (CoQ10) alone as well as in combination with Vitamin E derivative, Trolox against retinoblastoma cell line Y79 was assayed on normal human retinal pigment epithelium cells (ARPE-19) and Y79 cells using CCK-8. Apoptosis, cell cycle, ROS, and mitochondrial membrane potential (MMP) were measured by flow cytometry. The underlying mechanism of action was unraveled by western blotting. In order to substantiate the antiangiogenic effect of the combination Y79 cells were cocultured with HUVEC cell line in presence as well as absence of CoQ10 and Trolox. Significant decrease in HUVEC cell viability was observed in presence of CoQ10 and Trolox primed Y79 cells. Highly apoptotic Y79 cells were seen when subjected to both CoQ10 alone as well as CoQ10 + Trolox, understood to be a consequence of excess ROS generation in cancer cells which can be further attributed to the breakdown of MMP. Cell cycle arrest was observed in the G2/M phase by both CoQ10 alone as well as CoQ10+ Trolox. CoQ10 alone could significantly reduce the phosphorylation of ERK and Akt, but when combined with Trolox, it could also reduce the expression of VEGFA. Further antiangiogenic potential of the combination was strengthened by testing in an in vivo model through Chorio allantoic membrane (CAM) assay.

The results suggest that CoQ10 when used alone or in combination with another antioxidant like Trolox could induce apoptosis in Y79 cells via inhibition of the ERK/Akt pathway and inhibit expression of VEGFA. This is the first-ever report on the in vitro anti-cancer potential of CoQ10 alone or when combined with Trolox on human retinoblastoma Y79 cell

**Biography:**

**Dr. Madhumita P. Ghosh**, born on 11<sup>th</sup> July 1971 completed Ph.D at Jadavpur University, Kolkata with UGC fellowship. She went to **National Eye Institute, NIH, USA as post doctoral fellow** to work on lens and cataract biology. Her journey at NIH was remarkably successful with publications in peer reviewed journals of Experimental Eye Research, Toxicology research, Investigative Ophthalmology and Visual Science and Molecular Vision. She developed passion for eye research and continued as **post doctoral fellow at National Brain Research Center, Manesar, India**. Then she moved to Amity University as faculty and submitted proposal to Govt of India for funding to establish a research lab and independent research group. Students joined in her DBT and DST funded projects worth 27 Lakhs and 47 lakhs respectively as fellows for Ph.d, developed animal models of glaucoma, diabetic retinopathy and well equipped in vitro cell culture laboratory. They are presenting papers in national and international conferences and publishing papers in scopus and web of science indexed journals. Her research group got recognition

from all the funding agencies including ICMR sanctioning Senior research fellowship for one of the student and submitted three patents in an year with complete data. Presently also working on regeneration of retinal ganglion layer from invtro grown retinal precursor cells of neonatal pups.