Role of the Transcription-independent Mitochondrial p53 Pathway to Centchroman Induced Apoptosis in Human Breast Cancer Cells (HBCCs) Cells

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Aims: *Centchroman (CC) has been established as a potent antineoplastic agent in Human Breast Cancer Cells (HBCCs) previously by us (1, 2). This study was done to further elucidate transcription-independent mitochondrial p53 pathway involved in its antineoplastic action.*
Methodology: *MCF-7 Human Breast Cancer Cells were used for the study. Tamoxifen (TAM), a widely used antiestrogen was employed as a positive control. To detect cytochrome c release, cytosolic and mitochondrial fraction of cells were separated. Caspase-9, and cytochrome c were evaluated by Western blot analysis and b-actin served as the loading control. Mitochondrial Membrane Potential (Δψm) was measured by the uptake of Rhodamine 123 (Rh 123) as a function of Δψm.*
Key findings*: Cytochrome c is involved in the possible mitochondrial membrane potential dissipation (1) as revealed by migration from mitochondrial fraction to the cytosol. We further revealed that p53 played a crucial role in Centchroman induced early apoptosis, with p53 protein rapidly translocated into mitochondria. Using pifithrin-a (PFT), a p53's mitochondrial translocation inhibitor, we found that pretreatment with PFT, Centchroman induced mitochondrial p53 translocation was significantly suppressed, accompanied by a significant alleviation in the loss of Δψm, cytochrome c release and caspase-9 activation*
Significance: *Conclusively, these findings indicate the contribution of the transcription-independent mitochondrial p53 pathway to early apoptosis in HBCC cells induced by Centchroman.*

References

[1] Nigam M, et al. Life Sciences 2008, 82(11-12):577-590.
[2] Nigam M, et al. Life Sciences 2010, 87: 750-758.