

# World Congress on Breast Cancer

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## Cross-talk between ER stress and the MEK/ERK pathway potentiates apoptosis in human triple-negative breast carcinoma cells: Role of a dihydropyrimidone, Nifetepimine

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Triple negative breast cancers (TNBC) are among the most aggressive and therapy resistant breast tumors and currently possess almost no molecular targets for therapeutic option in this horizon. In the present study we discerned the molecular mechanisms of potential interaction between ER stress response and the MEK/ERK pathway in inducing apoptosis in TNBC cells. Here we observed that induction of ER stress alone was not sufficient to trigger significant apoptosis but simultaneous inhibition of the MEK/ERK pathway enhanced ER stress induced apoptosis via a caspase dependent mechanism. Our study also demonstrated nifetepimine, a dihydropyrimidone derivative as a potent anti-cancer agent in TNBC cells. Nifetepimine down-regulated MEK/ERK pathway in MDAMB-231 and MDAMB-468 cells and resulted in blockage of ER stress mediated GRP78 up-regulation. Detailed mechanistic studies also revealed that nifetepimine by down-regulating pERK expression also declined the promoter binding activity of TFII-I to the GRP78 promoter and in turn regulated GRP78 transcription. Studies further extended to *in vivo* Swiss albino and SCID mice models also revalidated the anti-carcinogenic property of nifetepimine. Thus our findings cumulatively suggest that nifetepimine couples two distinct signalling pathways to induce the apoptotic death cascade in TNBC cells and raises the possibility for the use of nifetepimine as a potent anti-cancer agent with strong immune-restoring properties for therapeutic intervention for this group of cancer bearers.

### Biography

Parimal C. Sen, received his Ph.D. from Calcutta University; Post Doctoral training in USA. Joined Bose Institute in December 1983. Served as Chairman in the Departments of Chemistry, Microbiology and Molecular Medicine. Visiting Professor at Cornell University (1989-1991). He is a Fellow of the National Academy of Sciences, India and a Fellow of the West Bengal Academy of Science and Technology. Recipients of several national awards. Published almost hundred papers Internationally high impact journals. Major research interest- drug – protein, protein-protein interactions and their role in the regulation of ion transporting enzymes and protein kinases to develop drug(s) against cancer.

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