Background: Since most cancers are the result of dysregulation of the balance between apoptosis and survival pathways, combination treatments that can target gene products of these pathways at physiological doses are needed for cancer prevention and treatment. Curcumin, an active ingredient of Indian spice turmeric has been shown to interact with and modify the expression of AKT, a survival pathway protein in breast cancer cells. Our laboratory has shown that HIV protease inhibitor (HIV-PI) Nelfinavir can also down regulate pAKT expression and survival of breast cancer cells at physiological doses. However, chronic exposure of Nelfinavir has been shown to induce insulin resistance in HIV patients and most likely will do the same in breast cancer patients. Present study thus sought to determine if use of chemo preventive agent curcumin in conjunction with Nelfinavir will further lower the required doses of each of these drugs to modulate the survival kinetics of breast cancer cells thereby underscoring their usefulness in chemo preventive settings.

Methods: To achieve these objectives we will examine the effects of curcumin alone and in combination with Nelfinavir (Nel) on growth of human breast cancer cell lines MCF-7 and MCF-7dox using the classical MTT assay. The dose/concentration associated with 50% inhibition (IC$_{50}$) will be determined for curcumin and Nel (individually) on both cell lines. After treatment (48h) with curcumin at its IC$_{50}$ concentration, cells will be treated with Nel at its IC$_{50}$ concentration to determine if it results in increased inhibition (compared to individual treatments). To evaluate if this inhibition may be the result of increased ATPase pump activity, calcein efflux assays will be conducted in the presence of IC$_{50}$ concentration of both drugs. In addition since polymeric nanoparticles (NPs) are efficient in encapsulating hydrophobic drugs and can provide high loading capacity, liposomal formulations of both of these drugs will also be tested in the same assays.

Conclusion: Our studies are focused on the deduction of a formulation of combination therapy that is effective in chemo preventive setting with a delivery system that is highly efficient and reproducible.

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