Title: Design And Development Of A Novel Series Of ER Ligands And Fluorescent Imaging Of Intracellular Analytes In Cancer Cells

Abstract:

Non-steroidal compounds based on triphenylethylene structure resembling 4-hydroxytamoxifen (4-OHT) (active metabolite of tamoxifen) were designed as inhibitors for targeting estrogen receptor alpha (ERα). A computer-aided strategy was used to design a library of molecules having structural similarity with 4-OHT. After energy minimization, the lead molecules were subjected to docking process with ERα. Molecular dynamics study was also used to obtain the globally minimized state of ligand and receptor. Details about the design and development of the lead molecules and their optimisation process have been discussed. We have reported a new family of bis-arylidene oxindole and methyl jasmonate derivatives, which shows highly selective estrogen receptor (ER)-mediated anticancer activity at low-micromolar concentrations in ER-positive (ER+) breast cancer cells. In order to determine the biological pathways, these molecules are labeled with some fluorescent markers and their biological evaluation is underway to expand our knowledge in optimizing the pharmacophore with improved potential.

Some unique FRET molecules based on environmentally sensitive fluorophores were also developed for selective cancer cell imaging. These molecules give rise to emission at different wavelengths in presence and absence of analytes. We have used FRET technique to measure the concentrations of some important metal ions which are relatively less known in different cancer cells. Some other non FRET based fluorescent probes have also been designed and developed for selective detection of analytes in cancer cells. Luminescence bioimaging offers an exclusive advantage in visualizing morphological details of tissues with sub cellular resolution. It is a powerful tool for monitoring and investigating micro species in living cells. We have presented the general design principles of luminescent chemosensors for bioimaging and summarized recent advances in the detection of metal cations and amino acids in vitro. On the basis of the advantages and disadvantages of the present luminescent chemosensors used for bioimaging, several future directions in this field would be followed to develop better luminescent chemosensors and to exploit their future application.

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