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Development of mitochondria targeted nanocarrier conjugated drugs against breast cancer

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Background: According to the Global Cancer Report issued by the World Health Organization, there are over 10 million new cases of cancer each year and over 6 million annual deaths from cancer disease. Breast cancer among women is the most common cancer in the world. By 2030, more than 70% breast cancer patients will come from developing countries like India. The development of resistance to variety of genotoxic DNA damaging agents is one of the major challenges in effective and long lasting breast cancer treatment.

Aim: The ongoing research project aims for the development of mitochondria targeted nanocarrier conjugated drugs against breast cancer. The goal is to test nanocarrier-targeted system (PLGA-b-PEG-TPP) drug delivery and overcome breast cancer chemotherapy drug resistance by either simultaneous or sequential delivery of resistance inhibitors (e.g., proposed inhibitors against mitochondrial telomerase and DNA ligase III).

Methods: Altered mitochondrial function and DNA metabolisms in the presence or absence of mitochondria targeted inhibitor and genotoxic drugs were investigated. Currently, new combinatorial anti-cancer drug therapy using nanocarrier conjugated telomerase inhibitor (Rubromycin and EpigallocatechinGallate), DNA Ligase inhibitor (L189) and chemotherapeutic DNA damaging drugs are being used. MCF-7 and MDA-MB-231 were used as in vitro breast cancer cell model.

Results: Significant enhancement in breast cancer cell death due to genotoxic drugs as cisplatin and doxorubicin in the presence of nanocarrier loaded mitochondrial DNA metabolizing protein inhibitors was found. Mitochondrial DNA metabolism was observed and its amount significantly decreased in breast cancer cell lines.

Conclusions: In conclusion, combinatorial drug therapy approach in case of breast cancer may prove to be an effective alternative approach to combat breast cancer drug resistance against chemotherapy drugs such as cisplatin and doxorubicin.

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