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A priori Activation of Apoptosis Pathways of Tumor (AAAPT) technology using natural tumor sensitizers for treatment of triple negative breast cancer patients

Statement of the Problem: Cancer cells have inherent ability to circumvent intervention irrespective of the nature of intervention by desensitizing themselves through a) activating survival pathways (e.g. NF-kB, PARP) and downregulating cell death pathways (e.g. CD95, ASK1) simultaneously. The situation is worse for Triple Negative Breast Cancer (TNBC) patients who have no option except non-specific chemotherapy, despite high off-target toxicity. No targeted therapy is approved for TNBC treatment since TNBC lack biomarkers (e.g. PR, ER and HER2 negative) for which drugs are designed. This puts TNBC patients' on an enormous risk for survival. The purpose of this study is to make FDA approved drugs better using Activation of Apoptosis Pathways of Tumor (AAAPT) technology.

Methodology & Theoretical Orientation: The proprietary AAAPT technology-based drug design utilizes natural tumor sensitizers derived from plants and/or human proteins and are targeted to cancer cells by using tumor specific biomarkers (e.g. Cathepsin B, SSTR2). The idea here is to revamp or inhibit specific signal pathways identified in the desensitization process.

Findings: The leading AAAPT drug molecules activated CD95 cell death pathway and inhibited NF-kB and PARP simultaneously and selectively in Cancer Stem Cells (CSCs) and in drug resistant tumor cells. The sensitizing potential of AAAPT drugs is reflected in the reduction of IC-50 of several front-line chemotherapeutics (e.g. Doxorubicin, Paclitaxel, Gemcitabine) by 10-15 times. As a result, the combination of AAAPT with chemotherapy achieved tumor regression in an in vivo xenograft TNBC tumor model at a much lower dose of chemotherapy and reduced dose resulted cardiotoxicity.

Conclusion & Significance: AAAPT synergizes with chemotherapy to make it clinically effective by reducing the side effects. The broader significance of AAAPT is that it can, potentially be used as a neoadjuvant to different therapeutic modalities including chemotherapy, radiation therapy, immunotherapy and radionuclide therapy and clinically translatable for a better management of cancer patients.

Biography

Raghu Pandurangi has completed his PhD in Spectroscopy followed by Post-doctoral training at Radiology and Internal Medicine, University of Missouri, Columbia where he remained as a Faculty researching on radiopharmaceuticals of cancer and cardiovascular diseases. He was a Team Leader at Mallinckrodt directing apoptosis imaging in 2004. He became an Entrepreneur in 2013 inventing AAAPT technology for improving FDA approved drugs. Currently, he is the Founder, President and CSO of Sci-Engi-Medco Solutions and Amplexi-LLC and recipient of several grants.

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