Chemo-radiotherapy versus standard radiotherapy in breast cancer – a computational and biological perspective

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Abstract

Breast cancer (BC) is the most prevalent cancer globally, accounting for 12.5% of all new cases reported each year. High overexpression of human epidermal growth factor receptor 2 (HER2, encoded by the ERBB-2 gene) is associated with more aggressive BC with a poor prognosis [1]. The therapeutic options for this type of cancer are surgery, adjuvant chemotherapy (CTx), radiotherapy (RT), hormonal, or targeted therapy. Chemotherapy and radiation therapy together have the potential to greatly enhance cancer treatment. Namely, proton therapy could enhance patient prognosis and preserving the healthy tissue by reducing irradiation of off-target tissue [2].

The aim of this study is to address a current medical challenge in cancer treatment using HER2 breast cancer as a model, taking advantage of the potential of viral-type particles as nanocarriers, delivering the chemotherapy agent directly to the target and so studying the synergetic effect of the chemotherapy agent with RT-induced ROS-mediated signals in cell receptors.

In the computational methodology, we will perform molecular dynamics (MD) simulations to understand the behavior of the VLP with the target and after how the interactions occur between the ROS produced and the VLP loaded and unloaded with the chemotherapeutic drug and the target. Firstly, we have studied the behavior of the chemotherapeutic drug in the VLP system. Molecular docking was performed with AutoDock Vina [3] using the structure of the VLP-HER2 receptor (PDB-ID:1N8Z) [4] and an optimized Doxorubicin structure. From the nine best complexes resultant from the docking the complex with better score was chosen to proceed with the 100 ns of MD simulation by GROMACS 2018.44 [5]. The simulation analysis was assessed by calculating RMSD, RMSF with GROMACS functions.

Experimentally, the expression of VLPs was assessed by enzyme-linked immunosorbent (ELISA) against HIV p24 and western blotting to detect the protein of interest (gp41). The therapeutic efficacy of photon-RT was assessed by evaluating cell viability *in vitro* in BC cell lines (MDA-MB-231, SK-BR-3, MCF-7 and MCF-10A). The first results suggest that, under the tested conditions,

there was no decrease in cell viability. Furthermore, a new experimental methodology regarding the production of VLPs is underway to achieve higher concentrations of the batches and survival assay in BC cell lines (MDA-MB-231, SK-BR-3, MCF-7 and MCF-10A) is ongoing to assess the biological effects from photon-RT.

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