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Research Article

In Silico Identification of Potential Inhibitors of the Wnt Signaling Pathway in Human Breast Cancer

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ABSTRACT

Triple-negative breast cancer is the leading worldwide cause of cancer-related deaths in women. The prospection and development of new substances with antitumoral potential is of great importance for the treatment of this disease. The objective of this work was to identify a commercial drug or ligand that could potentially bind to the FZD7 transmembrane protein and inactivate the Wnt signaling pathway in triple-negative breast cancer cells. We aimed at computationally modeling the FZD7, Wnt3, and Wnt3a proteins, at making them available in protein model databases, and at conducting docking analysis to assess the binding free energy between FZD7 and the selected ligands. The Wnt3 and Wnt3a proteins were modeled by homology modeling, and the FZD7 protein was modeled by homology modeling and ab initio modeling. The ligands were selected based on their similarity to the palmitoleic acid and were gathered from the ZINC database. A total of 30 commercially available ligands were found in the ZINC database. The docking results show that the ligands zinc08221009, zinc13546050, zinc05260769, zinc04529321, and zinc05972969 are good candidates for novel drug development. The created models and conducted analysis by this work will most certainly help in future research on the Wnt signaling pathway and its components.

Keywords: ab initio modeling, breast cancer, docking, homology modeling, Wnt signaling.

1. INTRODUCTION

BREAST CANCER is the world's leading cancer in women and the second most common cancer type in the world, representing more than 20% of new cases every year. Although of good prognosis when diagnosed early, with cure rates that can reach 90%, in Brazil, the mortality rates are still high, mostly due to late diagnosis. In developed countries, the 5-year survival rate after treatment is 85%, whereas in developing countries this rate drops to 70% (World Health Organization, 2017).

Triple-negative breast cancer cells (TNBC) do not have a therapeutic molecular marker. In this type of tumor there is the superexpression of the canonical and noncanonical Wnt signaling pathway, which contributes to cell transformation and tumor progression. This pathway is activated by ligands of the

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