ANALYSIS OF INTERACTION BETWEEN DESIGNED LIGANDS AND THE PROTEIN PPARγ USING DOCKING AND IN VITRO ASSAYS

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The nuclear peroxisome proliferator-activated receptors (PPARs) are important in many tissues due to their involvement in glucose and lipid metabolism. For this reason, alterations in their gene expression can lead to diseases like diabetes, atherosclerosis, hypertension, dyslipidemia and cancer, among others. PPAR suffers conformational change when binding to ligands derived from fat or lipid, which modulate PPAR's ability to bind with different co-factors. Therefore, the various functions of these proteins can be related to the diversity of ligands with which they interact. Because of their important role in metabolism, PPARs have been targeted with a variety of molecules in different diseases. The prospection of candidate molecules capable of interacting with PPAR can provide relevant alternatives to be applied in the treatment of such diseases. The aims of the present work were to characterize the interaction of PPARγ and compounds derived from anacardic acid and verify their antitumor properties. To do that, the interaction between PPARγ protein and the designed compounds was assessed through Autodock Vina docking program. Breast cancer cell (MD-MB-231) were treated or not with the designed compounds and cell viability was assessed by MTT assay and cell death was analyzed by annexin-PI staining followed by flow cytometry analysis. Our results demonstrated that ligands interact in two different regions (near residues Arg288 and Tyr473) and that most ligands (LDT11, LDT13, LDT15, LDT208, LDT380 and LDT383) can interact in both regions. Furthermore, three ligands (LDT28, LDT29 e LDT30) interact only in the region near Arg288 residue. In vitro experiments demonstrated that LDT11, LDT13, LDT380 and LDT383 promote reduction of cellular viability and induced apoptosis of breast adenocarcinoma cells. We concluded that ligands LDT11, LDT13, LDT380 and LDT383 have shown interesting properties to be considered leading molecules for drug-design against breast adenocarcinoma.

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