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Molecular docking approach to identify potential anticancer compounds targeting ALOX5 for the treatment of Pancreatic Cancer

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Arachidonate 5-lipoxygenase (ALOX5) is belongs to lipoxygenase family of enzymes. It metamorphose essential fatty acids substrates into leukotrienes as well as a wide range of other biologically active products. Pancreatic adenocarcinoma remains one of the most fatal animocity. The incidence of pancreatic cancer has steadily increased over the past four decades[1]. Almost 30% of patients with pancreatic cancer present with large, locally advanced tumors in the absence of distant metastases. Because surgical resection is frequently contraindicated by vascular invasion, locally advanced pancreatic cancer has a dismal prognosis with a 6-10-month median survival[2]. The majority of patients present with advanced disease at time of diagnosis resulting in a 5-year survival rate of 7%.Previous studies shown that 5-lipoxygenase (5-LOX) mRNA and protein are expressed in human pancreatic cancer cell lines and that triptolide treatment significantly down regulates 5-LOX expression. Furthermore, LOX inhibitors were found to block proliferation of human pancreatic cancer cells whereas the LOX metabolites 5-HETE and 12-HETE were found to stimulate cancer growth through activation of the p44/42 mitogen-activated protein kinase and PI3/Akt kinase pathways[3]. ALOX5 products, particularly 5-hydroxyeicosatetraenoic acid and 5-oxo-eicosatetraenoic acid, promote the proliferation of these ALOX5 aberrantly expressing tumor cell lines suggesting that ALOX5 acts as a pro-malignancy factor for them and by extension their parent tumors[4]. Thus, for deterrence and treatment of pancreatic cancer induction of 15-LOX-1 expression may be an attractive option for the.5-LOX-derived leukotriene in the pathogenesis of cancer[5][6].

The present appraisal is sought to identify a high affinity molecule targeting against ALOX 5 for the treatment of pancreatic cancer through molecular docking studies. 27 established compounds were obtained from various literature studies. The ligand compounds were further prepared using Schrodinger suit software[7]. Protein 3D structure of ALOX5 was obtained from Protein Data Bank(PDB) using PDB ID: 3V92[8] . Molecular docking studies was performed using flexible docking software, Molegro Virtual Docker[9][10]. The compound AM-679(Pubchem cid: 71308150), found to be the most effective compound which bound with ALOX5. Further studies can be perform on AM-

679 by employ molecular descriptors, Virtual Screening, ADMET, Pharamacophore, Pharmacokinetics studies etc.

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