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# In silico identification of novel PKC $\beta$ II inhibitors: ligand and receptor based pharmacophore modeling, virtual screening, and molecular dynamics study

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The Protein Kinase C  $\beta$ II (PKC $\beta$ II) belongs to conventional class of Protein kinase C enzyme and is preferentially activated during diabetic cardiomyopathy [1]. An effective inhibition of PKC $\beta$ II is the potential option to directly treat the diabetic cardiomyopathy. Till date only one selective PKC $\beta$ II inhibitor, ruboxistaurin reached phase III clinical trial for diabetic complications. Thus, there is an urgent need for exploring available chemical space for new PKC $\beta$ II inhibitors. The sequential virtual screening workflow based on ligand and receptor based query was followed to identify novel PKC $\beta$ II inhibitors. Three different strategies were followed for developing the ligand based model by HipHop module implemented in Catalyst, using: (I) three active and six moderately active compounds; (II) 17 active compounds; (III) docked poses of the compounds used in strategy (II). Receptor based query was developed based on the cocrystallised crystal structure of PKC $\beta$ II with 2-methylbisindolylmaleimide (2mBIM) using the Unity module of Sybyl7.1. The best hypotheses from both methods consist of six features *viz.* one hydrogen bond donor (D), two hydrogen bond acceptor (A), two hydrophobic-aromatic (HYD) and one ring aromatic (R). Virtual screening scheme based on these 3D hypotheses identified a few molecules with higher docking score than the existing inhibitors. In addition, comparative molecular dynamics (MD) simulation studies of uncomplexed PKC $\beta$ II and its complexes with 2mBIM, ruboxistaurin and newly identified compounds were performed to analyze the binding mode of the molecules. This study showed that complexed form of PKC $\beta$ II was more stable

than uncomplexed one during simulation period, and showed the stable H-bond formation with Glu421, Val423. This reveals the favorable interactions of identified compounds with PKC $\beta$ II.

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#### Reference

1. Murray NR, Baumgardner GP, Burns DJ, Fields AP: Protein kinase C isotypes in human erythroleukemia (K562) cell proliferation and differentiation. Evidence that beta II protein kinase C is required for proliferation. *J Biol Chem* 1993, **21**:15847-15853.

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