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Abstract

Type I Protein Arginine Methyltransferases catalyze the formation of Asymmetric Dimethyl Arginine (ADMA) residues by transferring methyl groups from S-Adenosyl-L-methionine to the guanidine groups of arginine residues in variety of eukaryotic proteins. In the previous studies it has been concluded that PRMT1 contributes the major type I protein arginine methyltransferases enzyme activity present in mammalian cells. ADMA is a naturally occurring inhibitor of NOS. It is clear that it is generated by many different cell types in the cardiovascular system and affects vascular and cardiac function. Correlation of ADMA with endothelial dysfunction and cardiovascular risk, together with the associations between cardiac risk factors and ADMA levels, suggest that ADMA is linked to cardiovascular disease, but strong causal relationships have yet to be established which qualifies it as a potential therapeutic target.

The induced fit of the active site upon binding of a known inhibitor was analyzed. The derived pharmacophore features were used to dock about 80000 molecules generated by ilib diverse in silico to the active site of the protein structure with Molegro Virtual Docker (MVD) program. Binding affinity of the lead candidates obtained by docking were compared to that of the known inhibitor and found to be much lower.

In this work a series of ten novel small molecules lead compounds were identified which could be developed into more effective therapeutic agents to modulate hypertension and control atherogenic diseases of heart associated with raised ADMA levels.