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EVALUATION OF AN INVERSE MOLECULAR DESIGN ALGORITHM IN A MODEL BINDING SITE FOR THE IN SILICO DESIGN OF A YEATS2 GENE BLOCKADOR FOR THE DEPLETION OF YEATS2 AND ITS INTERACTIONS BETWEEN YEATS DOMAIN AND ACETYLATED HISTONES FOR THE REDUCTION OF THE ATAC COMPLEX-DEPENDENT H3K9AC PROMOTER LEVELS TARGETING TO THE DEACTIVATION OF THE ESSENTIAL NSCLC GENES

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Computational molecular design is a useful tool in modern drug discovery. Virtual screening is an approach that docks and then scores individual members of compound libraries. In contrast to this forward approach, inverse approaches construct compounds from fragments, such that the computed affinity or a combination of relevant properties is optimized. We have recently developed a new inverse approach to drug design based on the dead-end elimination and A* algorithms employing a physical potential function. It has recently been identified that the YEATS domain as a novel acetyllysine-binding module regulating the functional importance of YEATS domain-containing proteins in human non-small cell lung cancer (NSCLC) for cancer cell growth and survival. YEATS2 binds to acetylated histone H3 via its YEATS domain. Here, we have discovered for the first time an in silico predicted and computer-aided molecular designed YEATS2 gene blockador for the reduction of YEATS2-containing ATAC co-localized complex with H3K27 acetylation (H3K27ac) promoters of actively transcribed NSCLC genes as a histone H3K27ac inhibitor that regulates a transcriptional program essential for NSCLC tumorigenesis by utilizing the MicrocrylaqTM cluster of algorithms for Large-Scale Protein-Ligand Docking experiments. Computational chemistry, NSCLC genes, Protein-Ligand Docking experiments, ATAC complex-dependent H3K9ac promoter, acetylated histones, docking, compounds libraries, MicrocrylaqTM cluster of algorithms.