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Computational Strategies for Discovering Positive Allosteric Modulators for A1AR Using Pharmacophore Modeling and Molecular Dynamics Insights

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The A1 adenosine receptor (A1AR), categorized as a G-protein coupled receptor, holds a pivotal role in the regulation of diverse physiological processes, encompassing neurotransmission, cardiac functionality, and immune responses. Manipulating the activity of A1AR has emerged as a promising therapeutic strategy for a spectrum of conditions, including neurodegenerative ailments and cardiovascular disorders. Positive allosteric modulators (PAMs) represent a compelling avenue for fine-tuning the receptor's activity in a controlled manner.

Given the widespread presence and involvement of A1AR in a multitude of physiological functions, it emerges as a prominent target for drug development across various disease categories. We present an efficacious pharmacophore model constructed for the virtual screening of possible PAM molecules. Our objective is to identify a set of compounds capable of establishing a robust interaction with the receptor, thereby influencing and regulating its activity. Furthermore, molecular dynamic simulations were utilized to gain insights into the dynamic behavior of molecules interacting with the receptor. This comprehensive exploration serves to enhance our comprehension of A1AR and paves the way for novel avenues in drug discovery endeavors targeting this receptor.