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Scientific article

The Potential of AlphaFold2-Predicted Adenosine Receptor Structures in Drug Discovery and Molecular Modeling

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Abstract. Adenosine receptors (ARs) have garnered attention as valuable targets in drug discovery due to their widespread expression across various tissues and their unique, tissue-specific roles. These receptors regulate numerous physiological processes, and drugs that selectively target ARs hold great therapeutic potential. Although several AR structures have been experimentally resolved and are available in structural databases like the Protein Data Bank (PDB), some receptor forms remain structurally undetermined. This gap limits the comprehensive molecular modeling needed to explore receptor-ligand interactions and accurately predict the potential therapeutic effects of candidate ligands. Recognizing the therapeutic promise of targeting adenosine receptors, we explored the feasibility of using AlphaFold2-predicted structures in drug design. Specifically, we examined the structure of the active A_{2B} AR predicted by AlphaFold2 and compared it with its experimentally determined PDB counterpart. Our analysis revealed a high degree of similarity, with a TM-score of 0.96 and a root mean square deviation (RMSD) of 1.48 Å, underscoring the viability of AlphaFold2 models for molecular docking and drug discovery applications. In addition, we performed comparative analyses of the active and inactive forms of A_{2B} and A_3 receptors and their associations with G-proteins. This assessment provided further insights into receptor functionality and structural dynamics, enhancing our understanding of their structure-activity relationships. Our findings support AlphaFold2 as a valuable tool in structural biology, especially for drug discovery targeting ARs, some experimental structures of which are unavailable. This approach holds promise for expanding *in silico* modeling possibilities, aiding in the development of specific and effective therapeutics.

Key words: protein structure prediction, TM-align, structural biology, structural analysis, drug discovery.

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Introduction

The A_{2B} adenosine receptor (AR) was initially identified and cloned in 1992 by Rivkees and Reppert from rat hypothalamus and Pierce et al. from human hippocampus tissue [1, 2]. The receptor's structure was classified as a typical G protein-coupled receptor (GPCR) with a molecular mass of approximately 36-37 kDa, and the subsequent studies confirmed its GPCR classification [3]. Despite being identified decades ago no high-resolution structure of A_{2B} AR has yet been obtained through X-ray crystallography [1, 2]. The only available experimentally determined structure to date is depicted in Figure 1 (published in the PDB on January 18, 2023, accession code 8HDO) and was determined using cryo-electron microscopy (cryo-EM), a less precise technique [4].

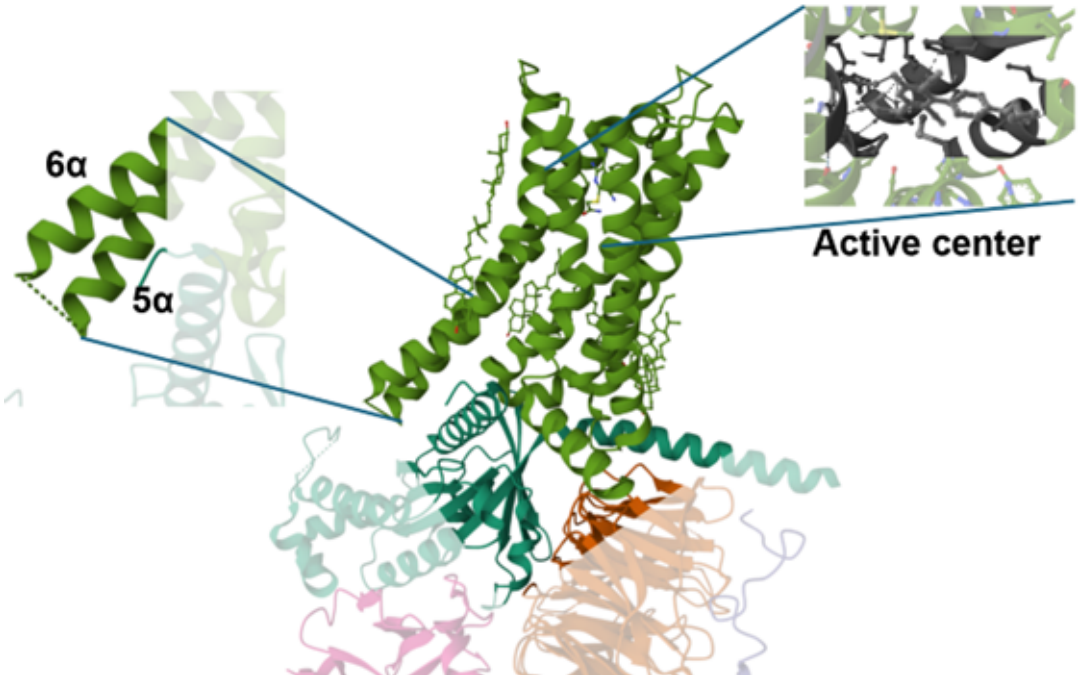

Figure 1. The structure of the active A_{2B} adenosine receptor (PDB accession code 8HDO) [4]. The structure of the A_{2B} chains is shown in green, and the structures of the G proteins are shown in other colors

Functionally, the A_{2B} AR primarily signals through the adenylate cyclase (AC) pathway, leading to elevated levels of intracellular cyclic adenosine monophosphate (cAMP) and activation of protein kinase A (PKA) and other cAMP-dependent effectors, such as the exchange protein Epac [5]. Additionally, A_{2B} AR can signal via the Gq-phospholipase C (PLC) pathway, which is connected to mitogen-activated protein kinase (MAPK) and arachidonic acid pathways. These pathways may regulate membrane ion channels via the $\beta\gamma$ subunits of the G protein.

A_{2B} AR is widely expressed in various cell types, including type II alveolar epithelial cells, endothelial cells, chromaffin cells, astrocytes, neurons, taste cells, and immune

cells such as mast cells, neutrophils, dendritic cells, macrophages, and lymphocytes [5]. Environmental factors like inflammation, cellular stress, injury, and hypoxia can modulate A_{2B} AR expression. For instance, interferon-γ increases A_{2B} AR transcription in mouse macrophages, TNF-α upregulates A_{2B} AR mRNA and protein in human colonic epithelial cells, and other mediators like IL-1β, reactive oxygen species, and endogenous adenosine further enhance its expression [6-10].

Despite the significant role of A_{2B} AR in cellular signaling pathways, the lack of high-resolution structural data poses challenges to fully understanding its activation mechanisms and interaction with potential drug candidates. While cryo-EM has provided a glimpse into the active state of A_{2B} AR, shown in Figure 1, the inactive form remains experimentally unresolved, limiting our ability to study both forms in parallel [4]. Structural insights into both states are essential, as they reveal critical details about receptor function and ligand binding, which are key for drug development. To address these gaps, recent advances in computational modeling, particularly through AlphaFold2, have enabled the prediction of both active and inactive protein structures, offering a new avenue for exploring GPCR conformations (https://gpcrdb.org/structure/homology_models) [11]. The AlphaFold2-MultiState model, which includes A_{2B} AR, now provides accessible predicted models for numerous human GPCRs, offering valuable insights for research and drug design [12,13].

Another important GPCR without an experimentally resolved structure is the A_3 AR. This protein consists of 318 amino acids and features a GPCR architecture [14]. The A_3 AR's C-terminal domain has multiple serine and threonine residues, which may act as phosphorylation sites and contribute to receptor desensitization following agonist binding [15]. A_3 AR shows high expression in liver, lung, and immune cells, with lower levels detected in the heart and brain [16, 17]. This receptor has attracted attention as a potential therapeutic target in inflammation, cancer, and cardioprotection [15]. Adenosine-based A_3 AR agonists have shown efficacy as antinociceptive agents in preclinical pain models and are under clinical trials for treating rheumatoid arthritis, psoriasis, and hepatocellular carcinoma [18, 19]. Additionally, heterocyclic-based A_3 AR antagonists are being studied for use in glaucoma and inflammatory airway diseases like asthma [20-22].

Understanding protein structures is fundamental in drug discovery, as it reveals critical details about how proteins interact with potential drug molecules. For GPCRs like the adenosine receptors, structural information is especially important, given their role in numerous signaling pathways related to various diseases. Detailed structural data enable researchers to analyze the binding sites, activation mechanisms, and potential conformational changes of these receptors, which are essential for designing effective and selective drugs. TheA_3 AR, despite its therapeutic potential, lacks experimentally resolved structures in both active and inactive states. Without this data, it remains challenging to determine precisely how this receptor could be targeted with new drugs. However, computational tools such as AlphaFold2 have helped fill this gap by predicting the active and inactive forms of A_3 AR, providing an initial model for study [23, 24]. Yet, because these structures have not been experimentally verified, their reliability for drug design remains uncertain.

An interesting approach to assessing the usability of these predicted structures is through the structural homology shared among adenosine receptors. Given that A_{2B} AR and A_3 AR share significant sequence and structural similarities, insights from A_{2B} AR structures may support and validate the use of A_3 AR models. This homology allows researchers to make cautious inferences about A_3 AR's predicted structure and its potential for ligand binding, aiding in the initial stages of drug discovery even for receptors without high-resolution data. This study aims to evaluate adenosine receptor structures predicted by AlphaFold2 alongside experimentally derived cryo-EM structures, determining their utility in drug design. Such an approach is particularly valuable for receptors like A_3 AR, where the identification of new ligands is hindered by a lack of structural data. By focusing on A_{2B} and A_3 AR, both of which hold significant promise for treating conditions such as inflammatory diseases and cancer, this study seeks to advance our understanding of using predicted structures as reliable models for drug discovery.

Material and Methods

Protein Structure Prediction with AlphaFold2

AlphaFold2, an AI-based algorithm, predicts protein structures from amino acid sequences with high precision [25, 26]. Its potential applications extend across various fields, including medicine, biology, and pharmaceuticals, facilitating more effective study of protein interactions and expediting new drug discovery [27]. Using deep learning techniques, AlphaFold2 generates initial protein folds and refines atomic-level structures. For prediction, it employs a multi-stage convolutional neural network to analyze amino acid sequences, predicting atomic pair distances and optimizing structural configurations based on energy constraints. The study used protein structures predicted by AlphaFold2-MultiState (https://gpcrdb.org/structure/homology_models) [11-14, 23, 24].

3D Structure Comparison and TM-Score Analysis

To assess and compare 3D protein structures, computational tools based on alignment algorithms, like DaliLite, VAST, and FATCAT, are commonly used [28]. These tools employ structural comparison algorithms that measure the similarity or difference between two protein structures. One key metric is the TM-score (Template Modeling score), calculated based on atomic contact analysis and enables structural alignment and similarity scoring [28]. For structural comparison, 3D protein models were sourced from the GPCRdb and RCSB PDB databases. Comparative structural analysis was performed using the TM-align tool (http://zhanglab.ccmb.med.umich.edu/TM-align/), which outputs TM-scores indicating structural similarity (0 to 1, where 1 implies identical structures). A TM-score below 0.5 typically suggests structural divergence. RMSD values were also provided, quantifying atomic deviations between structures, with lower RMSD indicating greater structural similarity [28].

Visualization of Structural Comparisons

To visualize and analyze 3D protein alignments, PyMOL software was utilized. This approach allowed the inspection of structural regions with key similarities and differences, facilitating an understanding of protein conformational variations in potential drug-target interactions.

Results and discussions

Comparative analysis of A_{2B} AR structures obtained by Cryo-EM and AlphaFold

For analysis, we used TM-align (version 20190822) with a statistical algorithm to align and compare protein structures: 0.0 < TM-score < 0.30 indicated random structural similarities; 0.5 < TM-score <1.00 indicated a high degree of similarity. The length of the reference A_{2B} structure obtained by cryo-EM was 280 residues, while the structure predicted by AlphaFold2 had 332 amino acid residues. The discrepancy in the amino acid residue count between the protein structures can be attributed to the inherent limitations of cryo-EM, which often exhibits poor resolution, potentially leading to the incomplete or absent visualization of certain structural elements. The alignment of the AlphaFold2-generated structure to the Cryo-EM structure was conducted. The structures were found to be almost identical, with a TM-score of 0.96143, indicating a similarity of 96% (Figure 2).

Visual analysis of the alignment revealed that the primary discrepancies are observed in the linkers that connect the α-helices. Figure 2 provides a clear visual representation of the structural differences between the AlphaFold2-predicted and experimental structures. Particularly, the AlphaFold2-predicted structure has a longer linker between the 4α and 5α helices compared to the experimental structure. Furthermore, analogous discrepancies are observed between the 5α and 6α, as well as the 6α and 7α structures. We attribute this discrepancy to the low resolution of Cryo-EM. More significant differences are observed in the intracellular helix 8α located in the C-terminal zone. This is attributed to the combination of the low resolution of Cryo-EM and the capabilities of AlphaFold2 in predicting protein structures. Nevertheless, visual analysis of the alignment demonstrated that the binding pocket in the two proteins is identical, as illustrated by the ligand bound to the reference structure. The ligand in question is adenosine, which has been demonstrated to function as a natural agonist of AR in several studies [3, 18, 29-31].

Furthermore, in order to ascertain whether there is a similarity or a difference between the two structures, we employed the parameter RMSD (Root Mean Square Deviation), which is a measure of the deviation between the corresponding atoms of the two structures. A smaller RMSD value indicates greater structural similarity. In the majority of cases, the RMSD is expressed in angstroms (Å). A comparison of the Cryo-EM-derived and AlphaFold2-predicted structures of A_{2B} revealed an RMSD value of 1.48, thereby confirming the similarity of the structures. Furthermore, the sequence identity was evaluated, resulting in a value of 0.989 (on a scale from 0 to 1, where 1 means 100% similarity). Therefore, we

demonstrated that the structures predicted by AlphaFold2 can be utilized further *in silico* experiments.

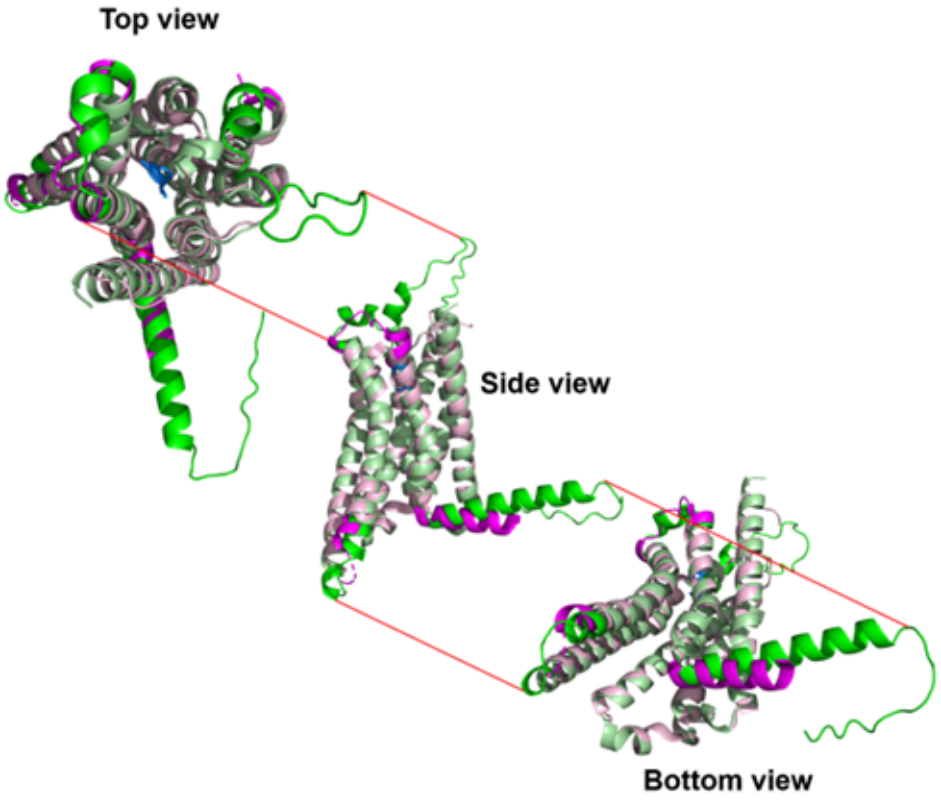

Figure 2. Visualization of structural comparisons between the active A_{2B} AR obtained by Cryo-EM (purple) with the ligand adenosine (blue) and the predicted active A_{2B} AR structure *AlphaFold2* (green). The intensity of the color shows the sites that differ between the two. The following views are provided for illustrative purposes: top view (extracellular region), side view (extracellular, intracellular, and transmembrane regions), bottom view (intracellular region)

To gain insight into the distinctions between active and inactive forms of adenosine receptors, we compared AlphaFold2-predicted active and inactive conformations of ARs. The TM-score of the aligned active and inactive conformations of A_{2B} AR yielded a value of 0.85, corresponding to 85% similarity. The RMSD was 2.91, and the sequence identity was 0.975, indicating that the structures are similar but nevertheless exhibit differences. The results of visual analysis with alignment showed that upon activation of A_{2B} AR, the part of the 1α chain directed to the extracellular space (N-terminal region) changes its location. This change is visualized in Figure 3. Possibly, after binding to the ligand, the protein conformation begins to change precisely from this chain. The active center begins to narrow, which leads to conformational changes in other α chains. A change in the location of 5α and 6α chains is also clearly visible. This change occurs on the side directed toward the intracellular space. In this case, the shift during activation occurs away from the central axis.

This change is necessary for dissociating from the Gs protein and activating the intracellular signal (this has already been shown for A_{2A} proteins) [32].

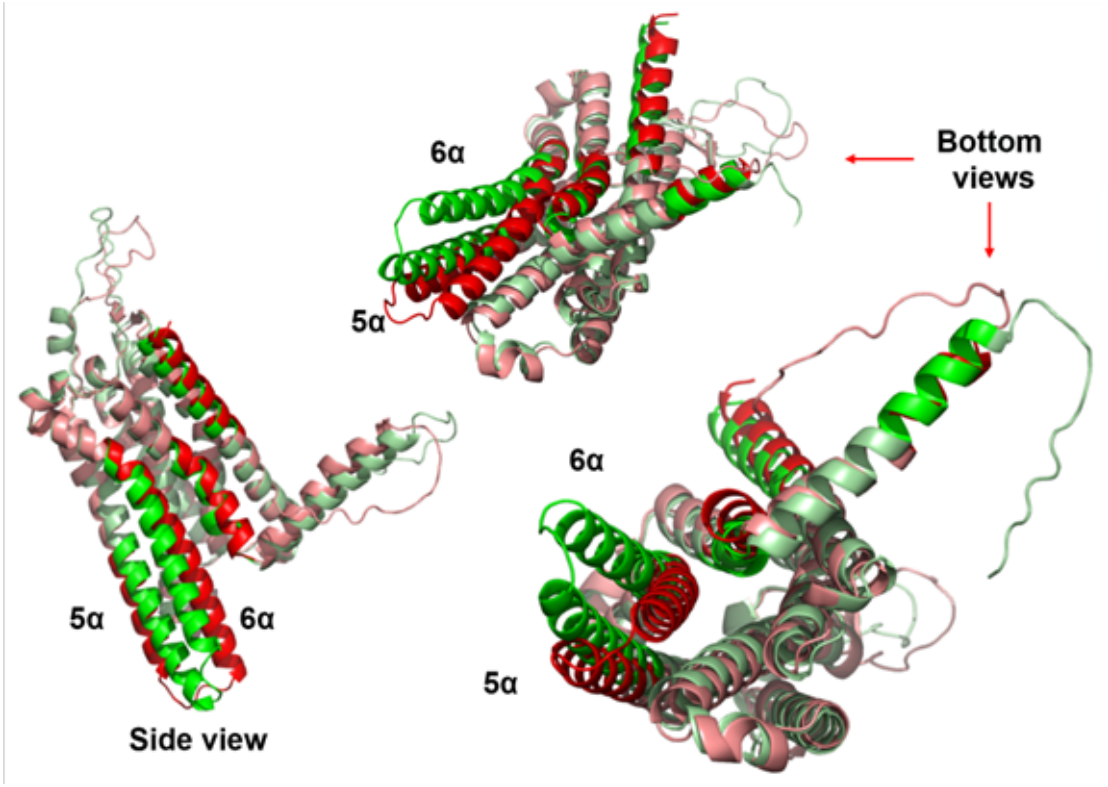

Figure 3. Visualization of the alignment of active (green) and inactive (red) A_{2B} AR predicted by AlphaFold2. The intensity of the color shows the sites that differ between the two. The following views are provided for illustrative purposes: side view (extracellular, intracellular, and intramembrane regions), bottom view (intracellular regions)

Furthermore, a structural analysis was conducted to examine the binding of both the active and inactive conformations of A2B to G-proteins. The visual representation of the relationship between receptor activation and association with Gs-protein is illustrated in Figure 4. The structural analysis images were generated in the PyMOL program by comparing the active and inactive A_{2B} structures, predicted by AlphaFold2, with the Cryo-EM-derived structure of the A_{2B} receptor bound to the Gs-protein. There is a minimal distinction between the 6α and 7α chains. It seems reasonable to posit that this change is necessary for the movement of the 8α chain, which is located in the interior of the cell. The 8α chain orientation affects modifications of the intracellular regions such as phosphorylation and ubiquitination after signal transduction by the Gs-protein [33].

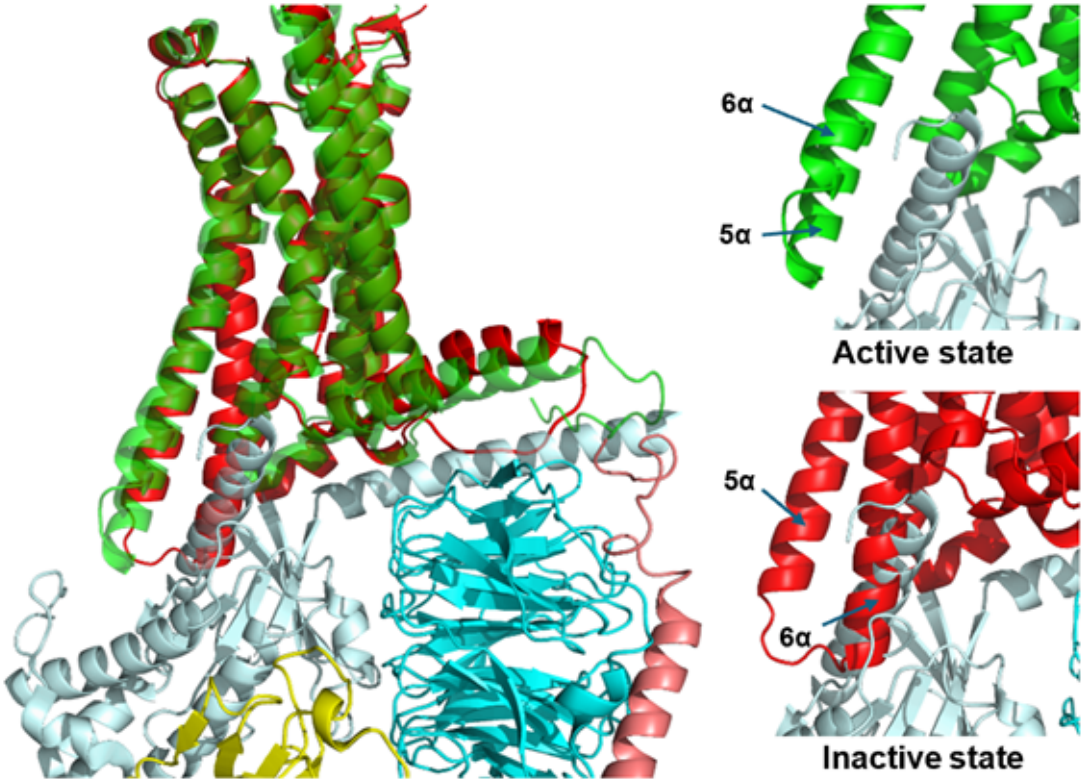

Figure 4. Changes in the arrangement of the 5α and 6α chains in the active (green) and inactive states of the A_{2B} AR (red) predicted AlphaFold2 with visualization of the Gα protein binding site (blue)

AlphaFold-predicted A3 AR conformational features

After assessing the similarity of the AlphaFold-predicted structure of the A_{2B} AR with the experimentally obtained structure of this receptor, an analysis was performed to determine the structural features of the AlphaFold-predicted A_3 AR in active and inactive conformations (Figure 5). TM-score of the aligned active and inactive conformations of A_3 AR showed a value of 0.92, which corresponds to 92% similarity. RMSD was 2.23, and sequence identity shows a value of 1.0, this indicates that the structures are similar but have large differences.

However, compared to A_{2B} in the active and inactive state (Figure 3), A_3 has fewer conformational changes (Figure 5). Visual analysis of the active and inactive A_3 receptor structures revealed similar changes, as those in the A_{2B} receptor. A similar change in the 1α chain is also observed in A_3. It is plausible that during receptor activation, the activation signal is transmitted starting from a change in the conformation of the 1α chain. Then, the 5α and 6α chains directed toward the intracellular space undergo a structure change, responsible for signal transmission through the G protein.

Similar changes are also shown in the transition from the 6α to the 7α and the 8α chain. These changes are necessary for further utilization of the receptor. However, in the A_3 active

structure, the changes in the 5α and 6α chains are less significant compared to the active A_{2B}. We explain this by the fact that A_3 binds not to the Gs protein, which affects the activation of AC, but to the Gi protein, which is responsible for inhibiting this membrane enzyme.

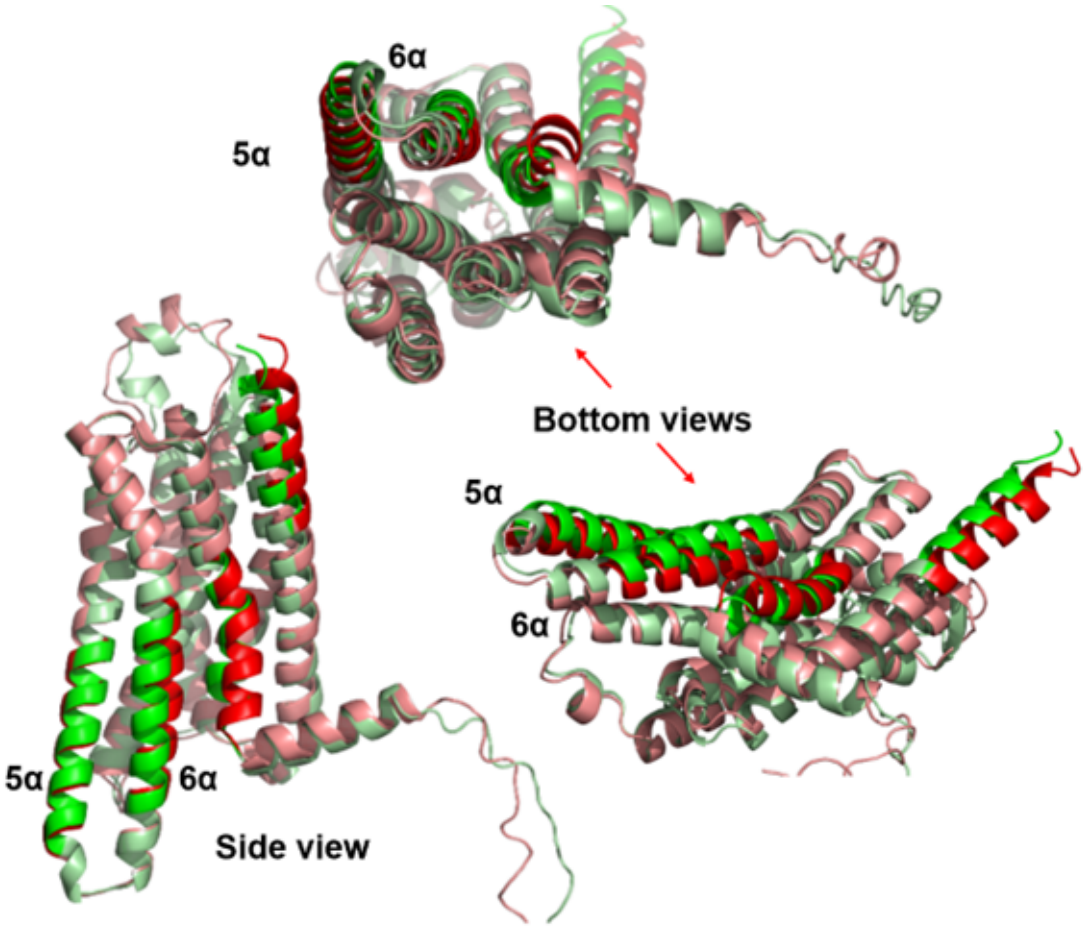

Figure 5. Visualization of the alignment of active (green) and inactive (red) A_3 AR predicted by AlphaFold2. The intensity of the color shows the sites that differ between the two. The following views are provided for illustrative purposes: side view (extracellular, intracellular, and intramembrane regions), bottom view (intracellular regions)

When attempting to conduct a structural analysis of the A_3 binding to the G protein, we encountered the previously described problem - no experimental structures of the A_3 adenosine receptor are available. The solution in this case was to test the interaction of A_3 AR with the Cryo-EM-derived structure of the Gi protein bound to A_1 AR [22,34]. Visualization of A_{2B} with the Gi protein of the A1 adenosine receptor is shown in Figure 6. As shown, for the activation of the Gi protein, fewer changes in the 5α and 6α chains are required compared to the activation of the Gs protein.

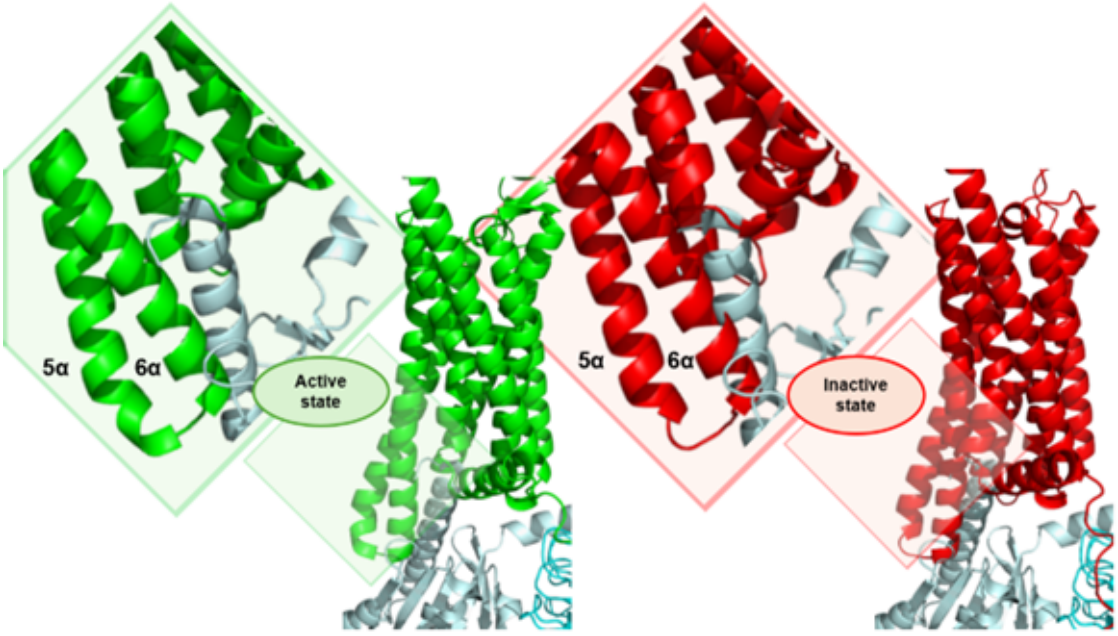

Figure 6. Changes in the arrangement of the 5α and 6α chains in the active (green) and inactive (red) states of the A_3 AR predicted by AlphaFold2, with visualization of the Gi protein binding site (blue)

Comparative analysis of AlphaFold-predicted active and inactive AR structures

To understand the structural changes of proteins associated with different G protein subtypes, we also performed TM-scoring and alignment of the structures of active A_{2B} with the active conformation of A_3 AR (Figure 7). TM-scores showed a value of 0.85 when using the active A_{2B} structure as a reference, which means that the similarity of the structures is 85%. However, when using the active A_3 structure as a reference, TM scores showed a value of 0.89, which corresponds to a similarity of 89%. RMSD calculation showed a value of 2.52, while sequence identity showed a value of 0.394, equivalent to a sequence similarity of 39.4%. This proves the differences between proteins in amino acid sequence and at the same time structural similarity.

Visual assessment of the differences and similarities between structures using alignment showed us very interesting results, which may be useful. The first similarity that was determined is in the α chains located in the bilayer of the membrane. This structure, as seen from the data shown above, is conserved between A_{2B} and A_3, and possibly all adenosine receptors. The main distinguishing feature between the structures of the two proteins, in our opinion, is the difference in the linkers between various α chains, such as between 2α and 3α, between 4α and 5α directed to the extracellular space. These sites are known to be amino acid sequences responsible for the primary binding to ligands. Considering the difference between the chains directed toward the intracellular space, the positions of 5α and 6α chains seem to distinguish GPCRs depending on their Gα types. Structural analysis of A_{2B} bound to Gs and A_3 bound to Gi are shown in Figures 4 and 6.

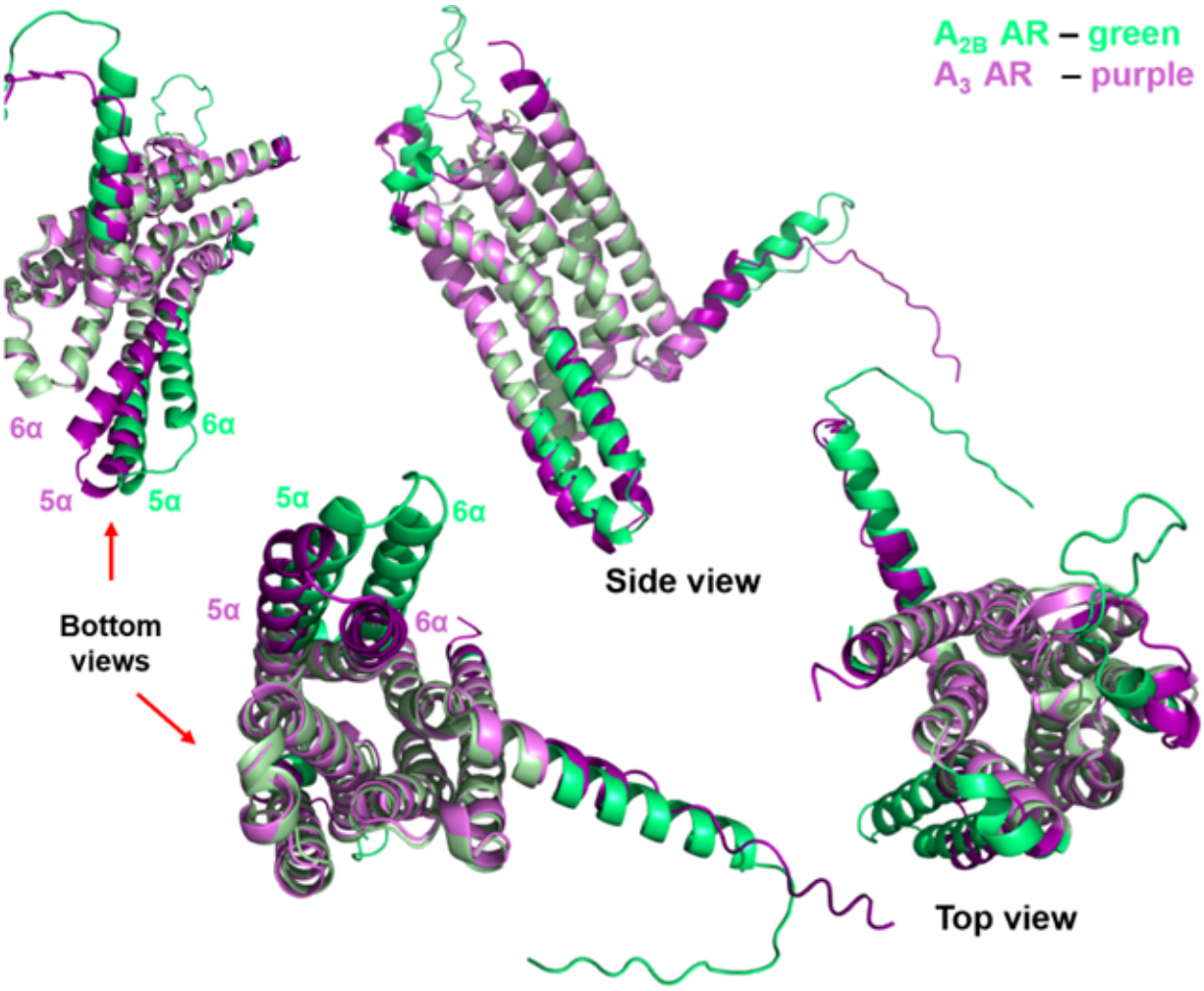

Figure 7. Alignment of the structures of active A_{2B} (green) with active A_3 (purple) ARs. The intensity of the color shows the sites that differ between the two. The following views are provided for illustrative purposes: top view (extracellular regions), side view (extracellular, intracellular, and transmembrane regions), bottom view (intracellular regions)

Additionally, a similar analysis was conducted for the inactive structures of A_{2B} with A_3 AR. TM-score when the A_{2B} structure was used as a reference was 0.87, and 0.90 when A_3 was used as a reference, which shows the identity of 87% and 90%. The RMSD value was 1.81, which indicates their greater similarity compared to the active states. In the inactive state, sequence similarity is almost identical, with a deviation of less than 1%, much less compared with the similarity between the active receptors (0.404, that is, 40.4%). Visual assessment of the difference and similarity of the structures by alignment showed that the inactive structures are almost identical (Figure 8). The main differences are the linker regions in the direction of the extracellular space.

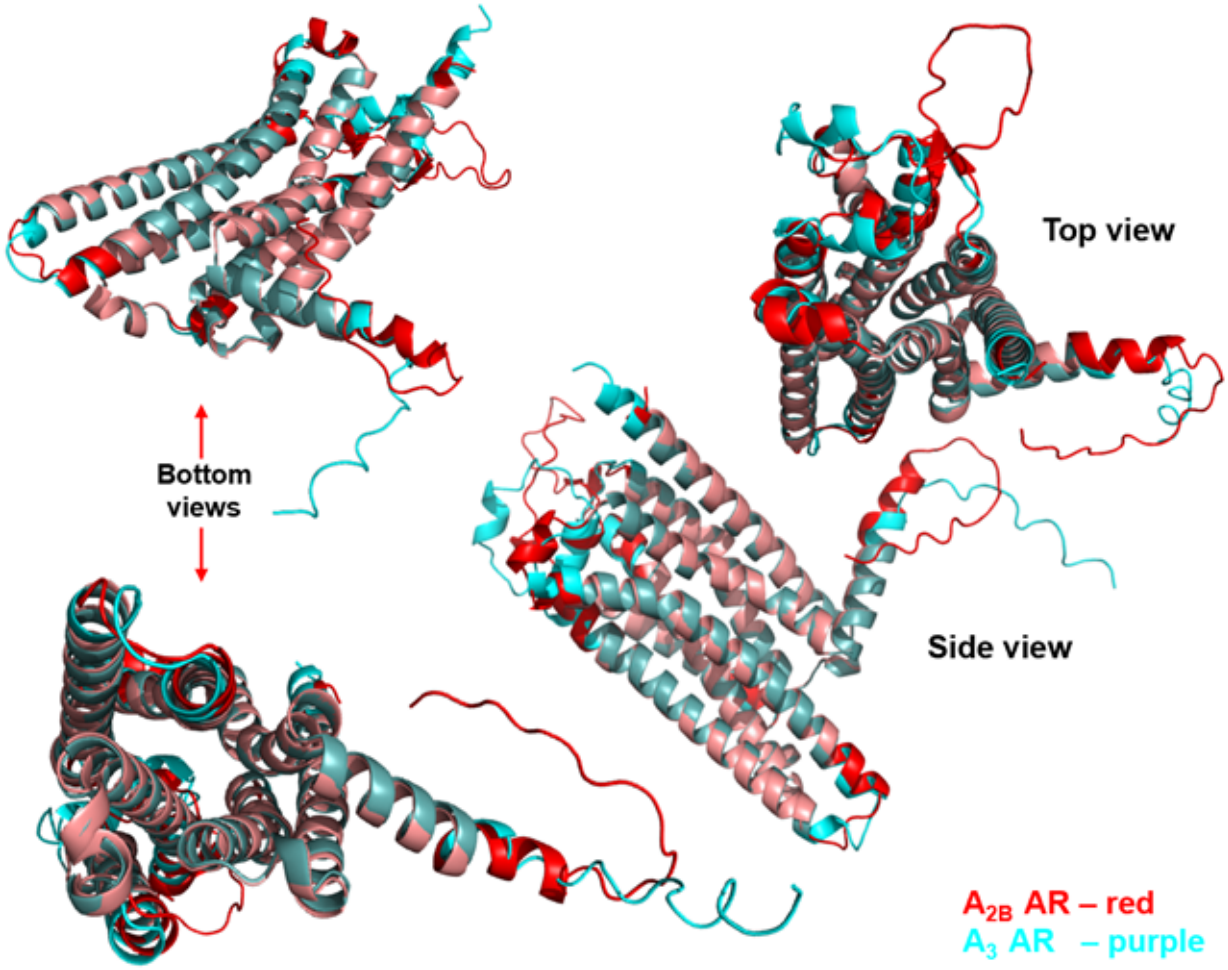

Figure 8. Alignment of the structures of inactive A_{2B} (red) with inactive A_3 (blue) AR. The intensity of the color shows the sites that differ between the two. The following views are provided for illustrative purposes: top view (extracellular regions), side view (extracellular, intracellular, and transmembrane regions), bottom view (intracellular regions)

Conclusion

During the study, we confirmed the relevance of using protein structures by the AlphaFold2 program. This study was done due to the lack of available A_3 AR and A_{2B} structures for molecular *in silico* research. According to our studies, the homology between the active structures of A_{2B} obtained experimentally and by modeling was 96%, with a sequence identity of 98%. We also conducted a comparative analysis of the active and inactive structures of adenosine receptors and determined regions that underwent changes under the influence of agonists. Structural analysis showed that α5 and α6 helices are responsible for releasing the Gα subunit. These data are supported by previous publications. Comparative analysis of the inactive forms of A_3 and A_{2B} AR showed structural homology from 87% to 90% with an amino acid sequence identity of 40%. Comparative analysis of the active forms of these

receptors showed homology of 85% to 89% depending on the reference protein, with an amino acid sequence identity of 40. However, visual analysis and also structural analysis showed that the release of Gαs, which is mediated by the A_{2B} AR signal, requires more conformational changes compared to the release of Gαi by the A_3 AR protein.

Source of funding

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Data Availability Statement

All the data are available within the manuscript.

Conflict of interest

The authors declare no conflicts of interest.

Authors' contribution

Satkanov M. – conceptualization, methodology, investigation, validation, data curation, writing – original draft, writing – review & editing, visualization.
Chupakhin E. – writing – original draft, writing – review & editing.

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Потенциал структур аденозиновых рецепторов, предсказанных AlphaFold2, в разработке лекарств и молекулярном моделировании

Аннотация. Аденозиновые рецепторы (АР) привлекли внимание как ценные цели при разработке лекарств из-за их широкой экспрессии в различных тканях и их уникальных, тканеспецифичных ролей. Эти рецепторы регулируют многочисленные физиологические процессы, и препараты, которые избирательно воздействуют на АР, обладают большим терапевтическим потенциалом. Хотя несколько структур АР были экспериментально

разрешены и доступны в структурных базах данных, таких как Protein Data Bank (PDB), некоторые формы рецепторов остаются структурно неопределенными. Этот пробел ограничивает всестороннее молекулярное моделирование, необходимое для изучения взаимодействий рецепторов и лигандов и точного прогнозирования потенциальных терапевтических эффектов. Осознавая терапевтические перспективы нацеливания на аденозиновые рецепторы, мы исследовали возможность использования структур, предсказанных AlphaFold2, при разработке лекарств. В частности, мы изучили структуру активного A_{2B} AP, предсказанную AlphaFold2, и сравнили ее с ее экспериментально определенным аналогом из PDB. Наш анализ выявил высокую степень сходства с оценкой TM 0,96 и среднеквадратическим отклонением (RMSD) 1,48 Å, что подчеркивает жизнеспособность моделей AlphaFold2 для молекулярной стыковки и приложений по поиску лекарств. Кроме того, мы провели сравнительный анализ активных и неактивных форм рецепторов A_{2B} и A_3 и их связей с G-белками. Эта оценка дала дальнейшее представление о функциональности рецепторов и структурной динамике, расширив наше понимание их структурно-активностных взаимосвязей. Наши результаты подтверждают, что AlphaFold2 является ценным инструментом в структурной биологии, особенно для поиска лекарств, нацеленных на AR, где экспериментальные структуры недоступны. Этот подход обещает расширить возможности моделирования in silico, помогая в разработке селективных и эффективных терапевтических средств.

Ключевые слова: прогнозирование структуры белка, TM-align, структурная биология, структурный анализ, поиск лекарств

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Дәрілік заттарды ашу және молекулалық модельдеу кезінде AlphaFold2 болжаған аденозиндік рецепторлар құрылымдарының әлеуеті

Аңдатпа. Аденозиндік рецепторлар (АР) әртүрлі тіндерде кең таралған экспрессиясына және олардың бірегей, тінге тән рөлдеріне байланысты дәрілік заттарды табуда құнды мақсат ретінде назар аударды. Бұл рецепторлар көптеген физиологиялық процестерді реттейді және АР-ға таңдамалы түрде бағытталған препараттар үлкен емдік әлеуетке ие. Бірнеше АР құрылымдары эксперименталды түрде шешілген және ақуыз деректер банкі (Protein Data Bank, PDB) сияқты құрылымдық дерекқорларда қол жетімді болса да, кейбір рецепторлардың пішіндері құрылымдық түрде анықталмаған күйде қалады. Бұл олқылық рецепторлар-лигандтардың өзара әрекеттесуін зерттеу және ықтимал емдік әсерлерді дәл болжау үшін қажет кешенді молекулалық модельдеуді шектейді. Аденозиндік рецепторларға бағытталған емдік уәдені мойындай отырып, біз дәрілік дизайнда AlphaFold2-болжамды құрылымдарды қолданудың орындылығын зерттедік. Атап айтқанда, біз AlphaFold2 болжаған белсенді A_{2B} АР құрылымын зерттедік және оны эксперименталды түрде анықталған PDB аналогымен салыстырдық. Біздің талдауымыз TM-балы 0,96 және орташа квадраттық ауытқуы (RMSD) 1,48 Å болатын ұқсастықтың жоғары дәрежесін анықтады, бұл AlphaFold2 модельдерінің

молекулалық қондыру және дәрілік заттарды табу қолданбалары үшін өміршеңдігін атап өтті. Сонымен қатар, біз A_{2B} және A_3 рецепторларының белсенді және белсенді емес формаларына және олардың G-белоктарымен байланыстарына салыстырмалы талдау жасадық. Бұл бағалау рецепторлардың функционалдығы мен құрылымдық динамикасына қосымша түсінік беріп, олардың құрылым-белсенділік қатынастары туралы түсінігімізді жақсартады. Біздің нәтижелеріміз AlphaFold2-ті құрылымдық биологиядағы құнды құрал ретінде, әсіресе эксперименттік құрылымдар қол жетімсіз АР-ға бағытталған дәрілерді табу үшін қолдайды. Бұл тәсіл in silico модельдеу мүмкіндіктерін кеңейтуге уәде береді, селективті және тиімді терапияны дамытуға көмектеседі.

Түйінді сөздер: белок құрылымын болжау, TM-align, құрылымдық биология, құрылымдық талдау, дәрілік заттарты зерттеу

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