Adenosine Receptor A2a

[Molecular Modelling and Drug Design]

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Outline

- Introduction
- Role of the Protein
- General Information of the Protein
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- Small Molecules / Ligands
- Diseases associated with the Protein
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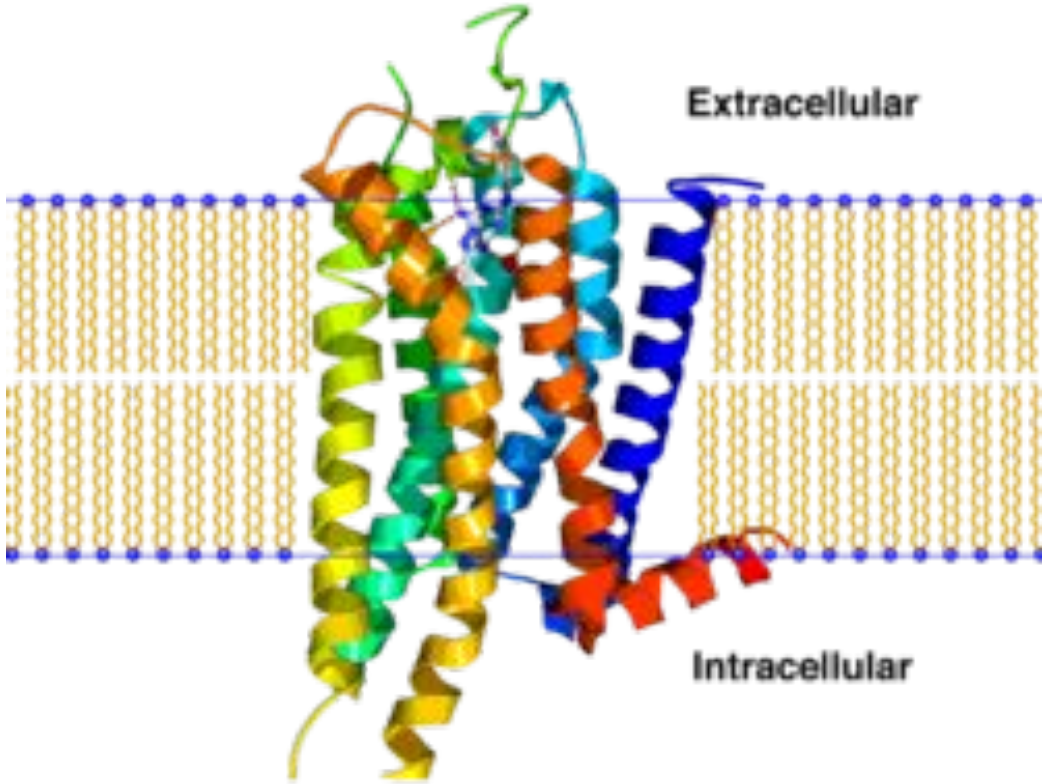
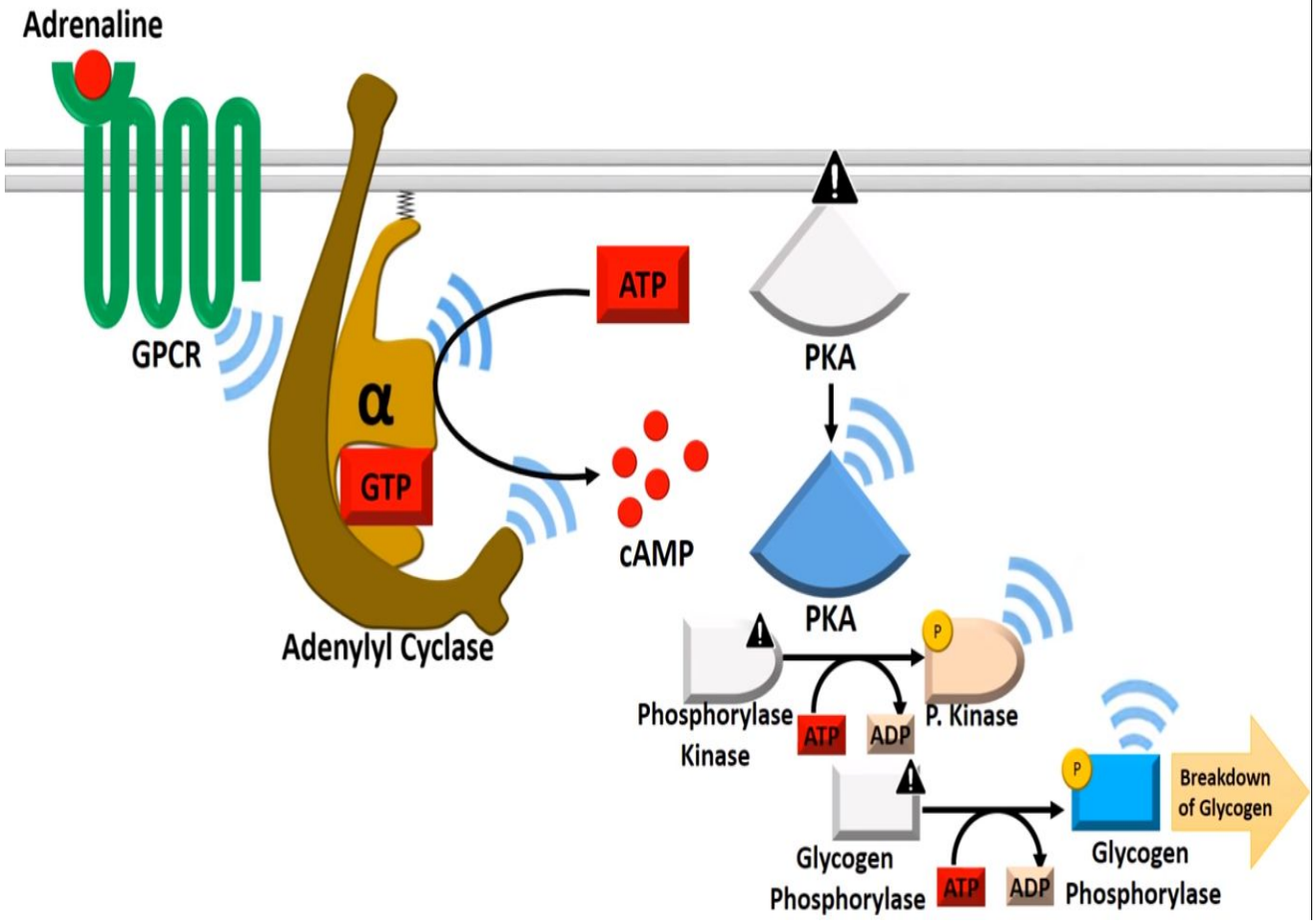
Introduction:

- The aim is to study the protein and its characteristics and help in drug designing exercise as a potential drug target
- Belongs to the family of G-protein coupled receptors.
- GPCRs are unique and are target of around 30% -50% of all modern medicinal drugs
- Ligands include light-sensitive compounds, pheromones, hormones, neurotransmitters, etc.



Role of the protein:

- Derivatives of adenosine play an important role in biochemical processes such as energy transfer as well as in signal transduction.
- All adenosine receptor subtypes (A1, A2A, A2B, and A3) are G-protein coupled receptors , classified based on their ability to either stimulate or inhibit adenylate cyclase activity.
- A_{2A} receptors are believed to regulate myocardial oxygen demand and to increase coronary circulation by vasodilation.
- It acts as a potential therapeutic target for brain-related conditions such as insomnia, depression, etc.

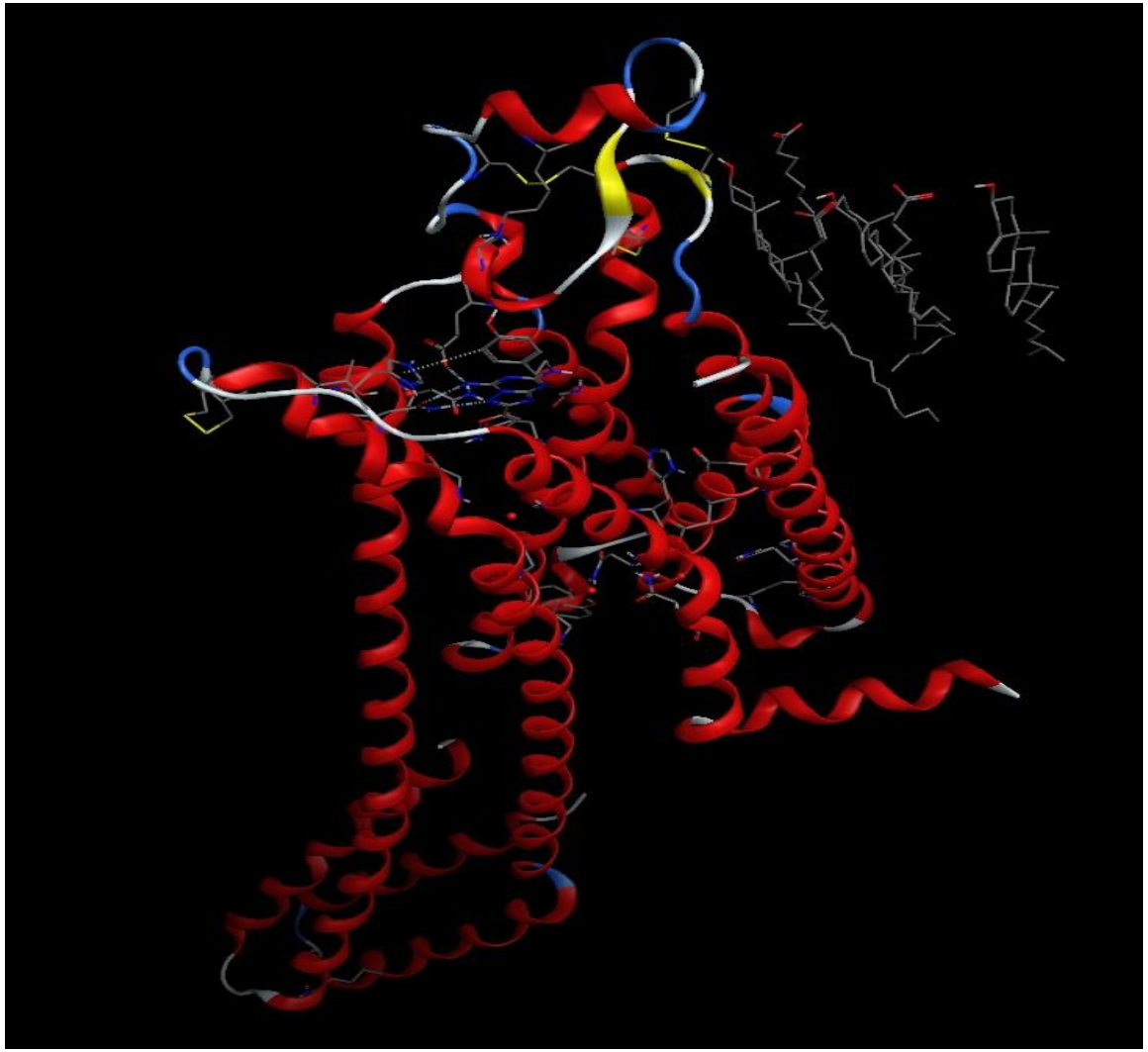


General Information of the protein

- Official Full Name: adenosine A2a receptor
- Official Symbol: ADORA2A
- Also Known as: A2aR; RDC8; ADORA2
- PDB ID: 5NLX
- Organism(s): E-coli, Homo sapiens
- DOI**:** 10.2210/pdb5NLX/pdb

- Experimental Data:
  Method: X-RAY DIFFRACTION
  Resolution: 2.14 Å
  R-Value Work: 0.199

- Chain Information:
  Polymer: 1
  Length: 433 residues
  Chain Type: polypeptide(L)
  Reference: UniProtKB (P29274)



Available XRD Structures

Total Count: 45

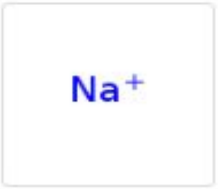
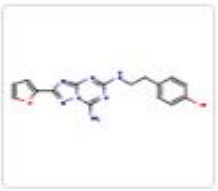
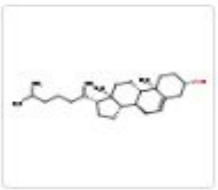
- X-Ray Resolution of 1.5 Å – 2.0 Å : 9
- X-Ray Resolution of 2.0 Å – 2.5 Å : 10
- X-Ray Resolution of 2.5 Å – 3.0 Å : 14
- X-Ray Resolution of 3.0 Å and more: 12

Ref: RCSB Protein Data Bank

Small Molecules / Ligands

Small Molecules

Ligands 4 Unique

ID	Chains	Name / Formula / InChI Key	2D Diagram & Interactions
NA Query on NA Download SDF File Download CCD File	A	**SODIUM ION** Na FKNQFGJONOIPTF-UHFFFAOYSA-N	
OLA Query on OLA Download SDF File Download CCD File	A	**OLEIC ACID** C_{18} H_{34} O_2 ZQPPMHVWECSIRJ-KTKRTIGZSA-N	
ZMA Query on ZMA Download SDF File Download CCD File	A	**4-{2-[(7-amino-2-furan-2-yl[1,2,4]triazolo[1,5-a][1,3,5]triazin-5-yl)amino]ethyl}phenol** C_{16} H_{15} N_7 O_2 PWTBZOIUWZOPFT-UHFFFAOYSA-N	
CLR Query on CLR Download SDF File Download CCD File	A	**CHOLESTEROL** C_{27} H_{46} O HVYWMOMLDIMFJA-DPAQBDIFSA-N	

Ref: RCSB PDB

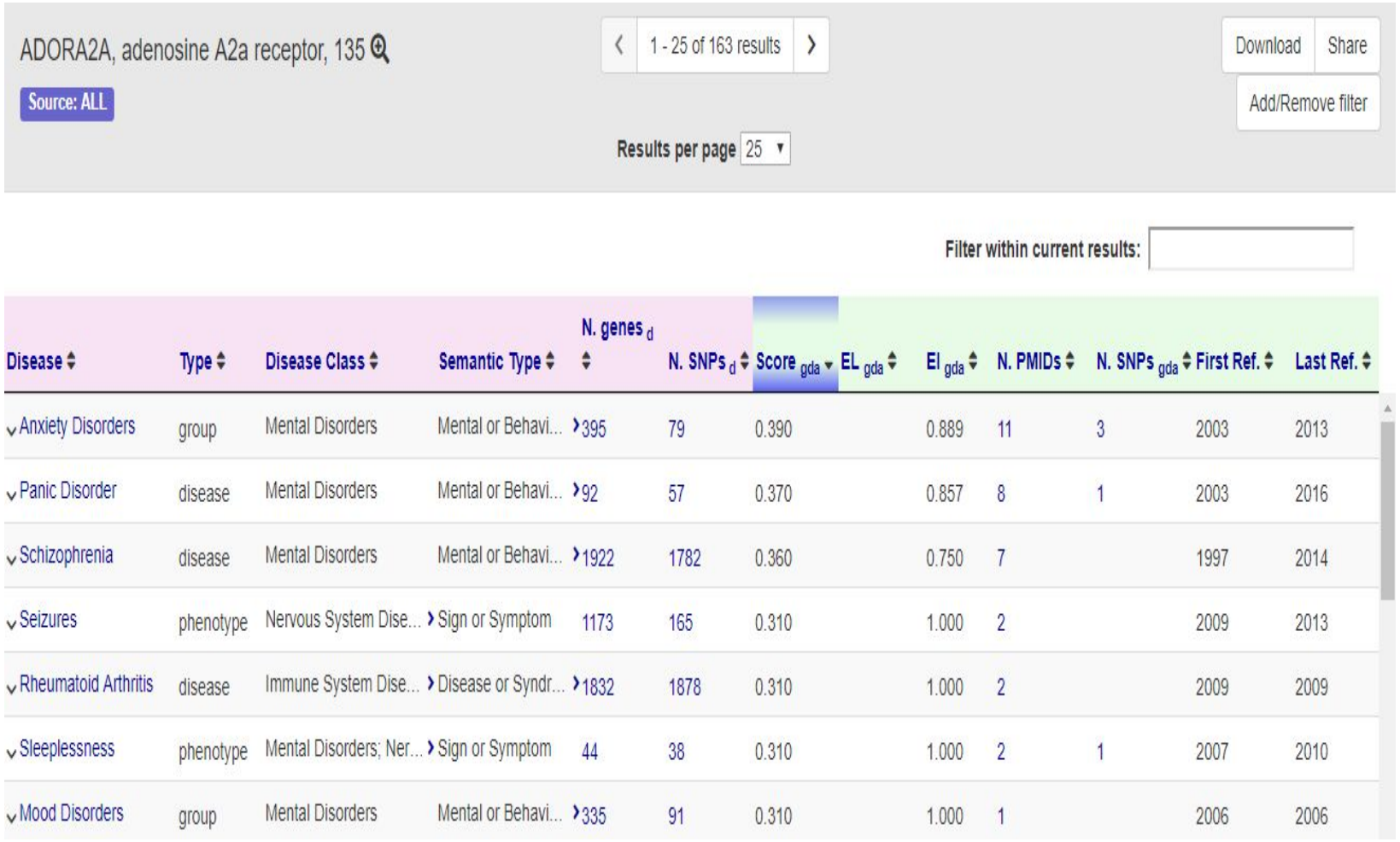
Diseases Associated with the protein

Total possible diseases associated with the protein : 163

Some Common diseases are:

- Anxiety disorder
- Panic disorder
- Sleeplessness
- Schizophrenia
- Seizures
- Tauopathies

Ref: DisGeNET



Disease	Type	Disease Class	Semantic Type	N. genes d	N. SNPs d	Score gda	EL gda	EI gda	N. PMIDs	N. SNPs gda	First Ref.	Last Ref.
Anxiety Disorders	group	Mental Disorders	Mental or Behavi...	395	79	0.390		0.889	11	3	2003	2013
Panic Disorder	disease	Mental Disorders	Mental or Behavi...	92	57	0.370		0.857	8	1	2003	2016
Schizophrenia	disease	Mental Disorders	Mental or Behavi...	1922	1782	0.360		0.750	7		1997	2014
Seizures	phenotype	Nervous System Dise...	Sign or Symptom	1173	165	0.310		1.000	2		2009	2013
Rheumatoid Arthritis	disease	Immune System Dise...	Disease or Syndr...	1832	1878	0.310		1.000	2		2009	2009
Sleeplessness	phenotype	Mental Disorders; Ner...	Sign or Symptom	44	38	0.310		1.000	2	1	2007	2010
Mood Disorders	group	Mental Disorders	Mental or Behavi...	335	91	0.310		1.000	1		2006	2006

Related Proteins

Total Count: 250
Ref: BLAST tool Uniprot

Overview

Collapse table

Entry	Protein names	Match hit (100 200 300 400 500 600)	Identity
P29274	**Adenosine receptor A2a** (Homo sapiens)		100.0%
X5DNB4	**Adenosine receptor A2** (Homo sapiens)		100.0%
A0A2J8IZL4	**Adenosine receptor A2** (Pan troglodytes)		100.0%
C9JQD8	**Adenosine receptor A2** (Homo sapiens)		100.0%
B4DW87	**Adenosine receptor A2** (Homo sapiens)		100.0%
B3KVQ4	**Adenosine receptor A2** (Homo sapiens)		99.8%
A0A2R9AR50	**Adenosine receptor A2** (Pan paniscus)		99.8%
A0A2J8IZJ6	**Adenosine receptor A2** (Pan troglodytes)		99.8%
A8K1F6	**Adenosine receptor A2** (Homo sapiens)		99.8%
G3RAD0	**Adenosine receptor A2** (Gorilla gorilla gorilla)		99.5%
			99.5%

Known Inhibitors / Approved Drugs for the protein

- Enprofylline - Inibitor
- Lamotrigine - Inhibitor
- Caffeine - Antagonist
- Theophylline - Antagonist
- Pentoxifylline - Antagonist
- Dyphylline - Antagonist
- Oxtriphylline - Antagonist
- 8-chlorotheophylline - Antagonist
- Regadenoson - Agonist
- Adenosine - Agonist

Ref: Drugbank

Conclusion

- Adenosine A2A receptor has been studied to aid in drug discovery process.
- The protein is extensively involved in major physiological processes in the living organism.
- The diseases associated with the protein mainly belong the nervous system disease category.

References

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- Daly JW, Shi D, Nikodijevic O, Jacobson KA. The role of adenosine receptors in the central action of caffeine. Pharmacopsychoecologia. 1994;7(2):201–213.

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Thank You!!