Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

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**Molekuláris bionika és Infobionika Szakok tananyagának komplex fejlesztése konzorciumi keretben

***A projekt az Európai Unió támogatásával, az Európai Szociális Alap társfinanszírozásával valósul meg.

BASICS OF NEUROBIOLOGY

Neurobiológia alapjai

METABOTROPIC RECEPTORS

(Metabotrop receptorok)

ZSOLT LIPOSITS

CHARACTERISTICS OF METABOTROPIC RECEPTORS

SYNONYM FOR METABOTROPIC RECEPTOR IS G PROTEIN-COUPLED RECEPTOR

THE BINDING OF THE LIGAND TO THE RECEPTOR RESULTS IN G PROTEIN ACTIVATION THAT TRIGGERS DOWNSTREAM EFFECTORS, MAINLY ENZYMES AND ION CHANNELS

THE G PROTEIN-COUPLED RECEPTOR FAMILY HAS MORE THAN 1000 MEMBERS

THE RESPONSE EVOKED VIA METABOTROPIC RECEPTORS HAS A SLOWER ONSET AND LONGER DURATION (FROM 0.1 s TO HOURS).

CERTAIN CLASSIC TRANSMITTERS UTILIZE BOTH THE FAST IONOTROPIC (RESPONSE TIME IS IN MILLISECONDS) AND THE SLOWER METABOTROPIC RECEPTORS FOR COMMUNICATION.

PEPTIDES USE G PROTEIN-COUPLED RECEPTORS EXCLUSIVELY

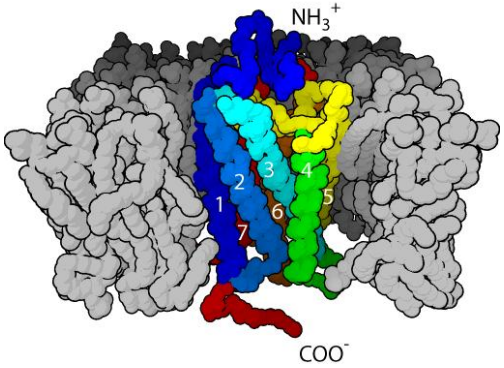
THE RECEPTORS BELONG TO SUBFAMILIES LIKE:

- METABOTROPIC GLUTAMATE TYPE
- RHODOPSIN-BETA ADRENERGIC TYPE
- SECRETIN-VIP TYPE

CHARACTERISTICS OF METABOTROPIC RECEPTORS

THE RECEPTOR POSSESSES 7 TRANSMEMBRANE DOMAINS

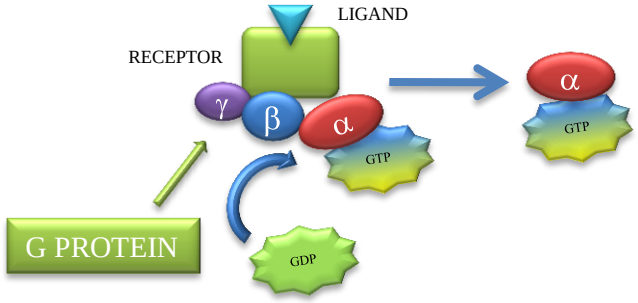
LIGANDS COMPRISE LIGHT-SENSITIVE COMPOUNDS, ODORS, PHEROMONES, HORMONES, NEUROTRANSMITTERS, PEPTIDES AND LARGER PROTEINS



THE ACTIVATED GPCR CAN TURN ON AN ASSOCIATED G-PROTEIN BY EXCHANGING ITS BOUND GDP FOR A GTP

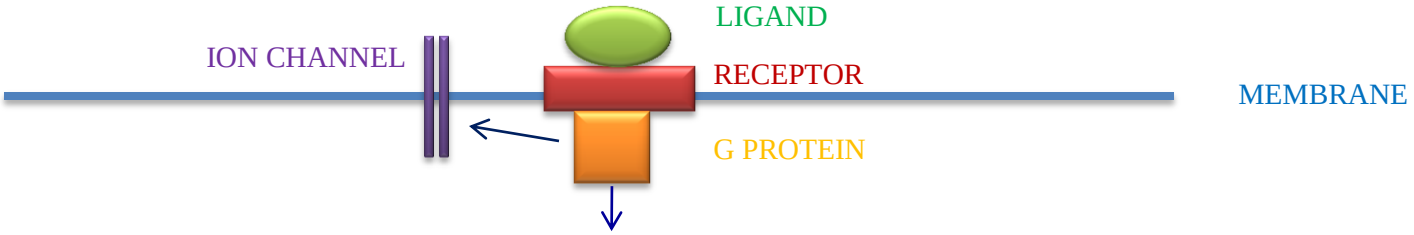
THE G PROTEIN HAS ALPHA, BETA AND GAMMA SUBUNITS. THE ALPHA SUBUNIT TOGETHER WITH THE BOUND GTP DISSOCIATES AND AFFECTS SECOND MESSENGERS

GPCRs UTILIZE cAMP AND PHOSPHATIDYLINOSITOL SIGNAL TRANSDUCTION PATHWAYS



G PROTEIN ACTIVATION BY LIGAND BINDING OF THE RECEPTOR

METABOTROPIC SIGNAL TRANSDUCTION



SECOND MESSENGERS
cAMP cGMP Ca^{2+} Diacylglycerol IP_3

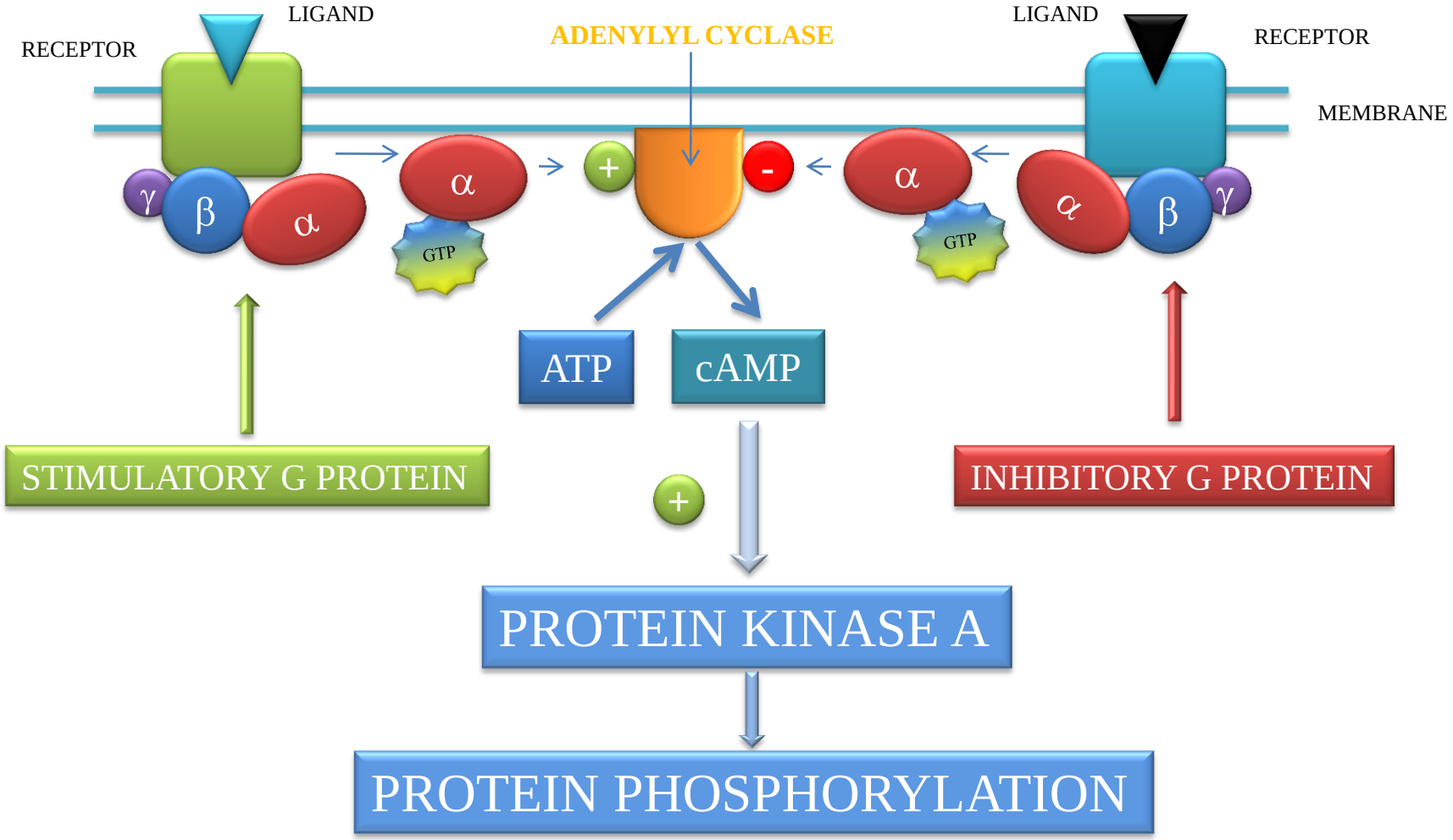
THIRD MESSENGERS
Protein phosphorylation

RAPID MEDIATORY EFFECT
Ion channel activation/inactivation

SHORT TERM MODULATORY EFFECT
General metabolism
Transmitter synthesis/release
Receptor sensitivity

LONG TERM MODULATORY EFFECT
Synthesis of receptors/channels
Synaptogenesis
Learning/memory

STIMULATORY AND INHIBITORY G PROTEIN ACTIONS



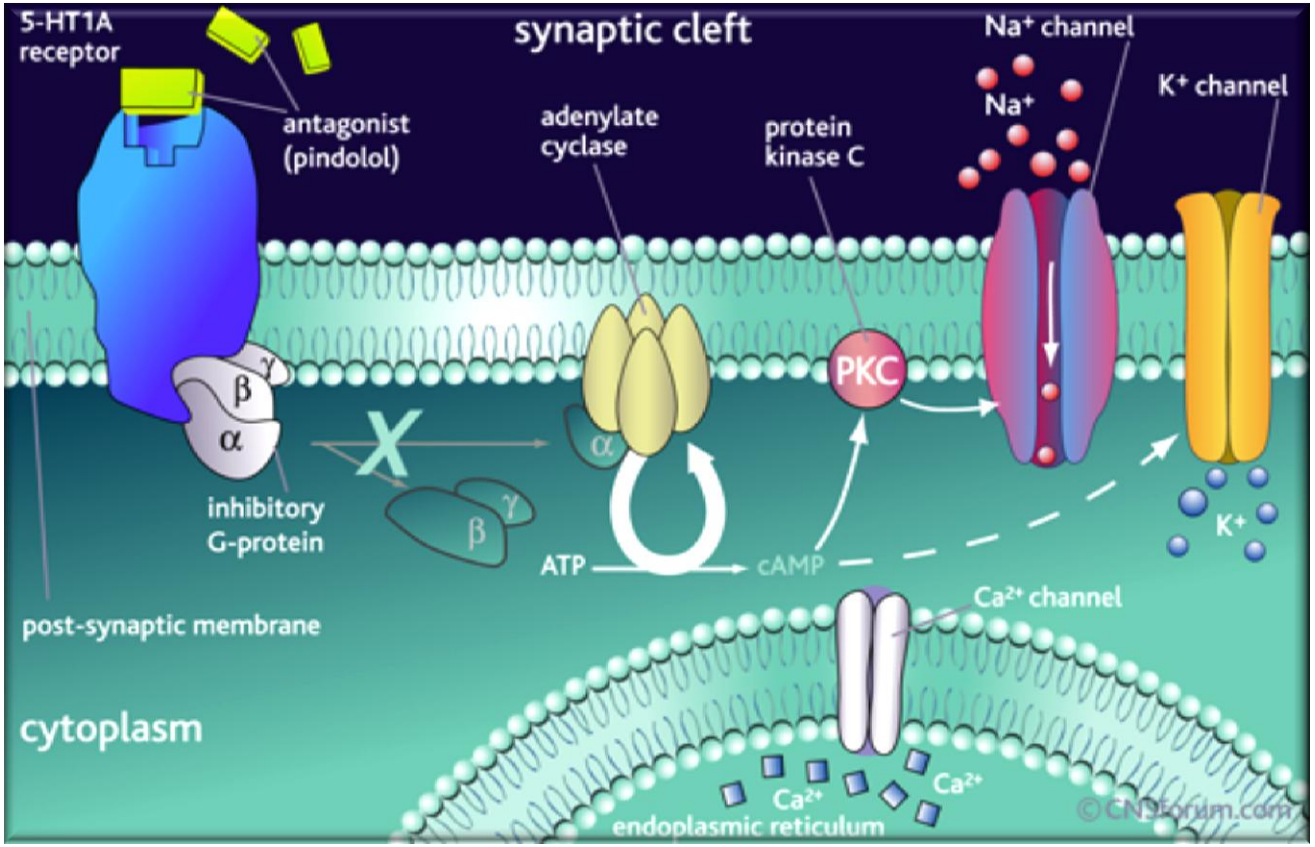
MUSCARINIC ACETYLCHOLINE RECEPTOR	
ATTRIBUTE	DESCRIPTION
NAME	MUSCARINIC ACETYLCHOLINE RECEPTOR
STRUCTURE	7 TRANSMEMBRANE
SUBTYPES	FIVE SUBTYPES HAVE BEEN DETERMINED, NAMED M1-M5
EXPRESSION TYPES	M1: CNS, EXOCRINE GLAND, M2: HEART, M3: SMOOTH MUSCLE OF BLOOD VESSELS. LUNG, M4, M5: CNS. PRE- AND POSTYNAPTIC RECEPTOR LOCATIONS IN THE BRAIN
LIGAND BINDING	HIGHER AFFINITY FOR MUSCARINE THAN NICOTINE
BASIC ROLE(S)	M1, M3, M5 COUPLE TO G PROTEINS THAT STIMULATE PHOSPHOLYPASE C M2, M4 COUPLE TO G PROTEINS THAT REGULATE POTASSIUM AND CALCIUM CHANNELS, INHIBIT ADENYLYL CYCLASE
AGONISTS	MUSCARINE, PILOCARPINE, BETANECHOL
ANTAGONISTS	ATROPINE, SCOPOLAMINE, PIRENZEPINE
FUNCTIONAL ROLES	REGULATION OF CNS NETWORKS AND AUTONOMIC NERVOUS SYSTEM
DISEASES	COGNITIVE DECLINE IN ALZHEIMER DISEASE DUE TO DIMINUTION OF ACETYLCHOLINE

METABOTROPIC GLUTAMATE RECEPTOR	
ATTRIBUTE	DESCRIPTION
NAME	METABOTROPIC GLUTAMATE RECEPTOR
STRUCTURE	7 TRANSMEMBRANE
SUBTYPES	EIGHT SUBTYPES DIVIDED INTO THREE GROUPS GROUP I: $mGluR_1$ and $mGluR_5$ Group II: $mGluR_2$ and $mGluR_3$ GROUP III: $mGluR_4$ and $mGluR_{6-8}$
EXPRESSION TYPES	WIDE DISTRIBUTION IN THE BRAIN, PRE- AND POSTYNAPTIC RECEPTOR LOCATIONS, INHIBITORY, PRESYNAPTIC AUTORECEPTORS
LIGAND BINDING	AT EXTRACELLULAR N TERMINUS PART OF THE RECEPTOR
BASIC ROLE(S)	GROUP I: STIMULATION OF PHOSPHOLIPASE (PLC) C GROUP II: INHIBITION OF ADENYLYL CYCLASE GROUP III: INHIBITION OF ADENYLYL CYCLASE
AGONISTS	2-CHLORO-5-HYDROXYPHENYLGLYCINE, (S)-3,5-DIHYDROXYPHENYLGLYCINE
ANTAGONISTS	4-CARBOXYPHENYLGLYCINE, 1-AMINOINDAN-1,5-DICARBOXYLIC ACID
FUNCTIONAL ROLES	REGULATION OF CNS NETWORKS
DISEASES	$mGluR_1$ INVOLVED IN SYNAPTIC PLASTICITY, LTP AND LTD

METABOTROPIC GABA RECEPTOR	
ATTRIBUTE	DESCRIPTION
NAME	METABOTROPIC GABA RECEPTOR (GABA B RECEPTOR)
STRUCTURE	7 TRANSMEMBRANE, LARGE SIMILARITY WITH THE METABOTROPIC GLUTAMATE RECEPTOR
SUBTYPES	TWO SPLICE VARIANTS ARE KNOWN ($GABA_BR_1$, $GABA_BR_2$)
EXPRESSION TYPES	WIDE DISTRIBUTION IN THE BRAIN, PRE- AND POSTYNAPTIC RECEPTOR LOCATIONS,
LIGAND BINDING	THE EXTRACELLULAR N TERMINUS PART OF THE RECEPTOR
BASIC ROLE(S)	ACTIVATION OF GABA B RECEPTORS LEADS TO AN INCREASE IN K^+ CONDUCTANCE, A DECREASE IN CA $^{2+}$ CONDUCTANCE AS WELL AS TO CHANGES IN THE LEVELS OF SECOND MESSENGERS (cAMP)
AGONISTS	BACLOFEN
ANTAGONISTS	SACLOFEN
FUNCTIONAL ROLES	REGULATION OF CNS NETWORKS
DISEASES	PAIN, EPILEPSY

METABOTROPIC SEROTONIN RECEPTOR	
ATTRIBUTE	DESCRIPTION
NAME	METABOTROPIC SEROTONIN RECEPTOR
STRUCTURE	7 TRANSMEMBRANE
SUBTYPES	13 SUBTYPES, CATEGORIZED INTO 6 GROUPS (5HT1, $5HT_2$, $5HT_4$, $5HT_5$, $5HT_6$,$5HT_7$)
EXPRESSION TYPES	WIDE DISTRIBUTION IN THE BRAIN
LIGAND BINDING	THE EXTRACELLULAR N DOMAIN OF THE RECEPTOR
BASIC ROLE(S)	INCREASING CELLULAR LEVELS OF cAMP: SUBTYPES 4,6,7 DECREASING CELLULAR LEVELS OF cAMP: SUBTYPES 1,5 INCREASING CELLULAR LEVELS OF IP3 AND DAG: SUBTYPE 2
AGONISTS	LARGE SCALE OF SUBTYPE SPECIFIC AGONISTS ARE KNOWN
ANTAGONISTS	LARGE SCALE OF SUBTYPE SPECIFIC ANTAGONISTS ARE KNOWN
FUNCTIONAL ROLES	REGULATION OF CNS NETWORKS
DISEASES	ANXIETY, AGGRESSION, ADDICTION, MOOD, MEMORY, SLEEP

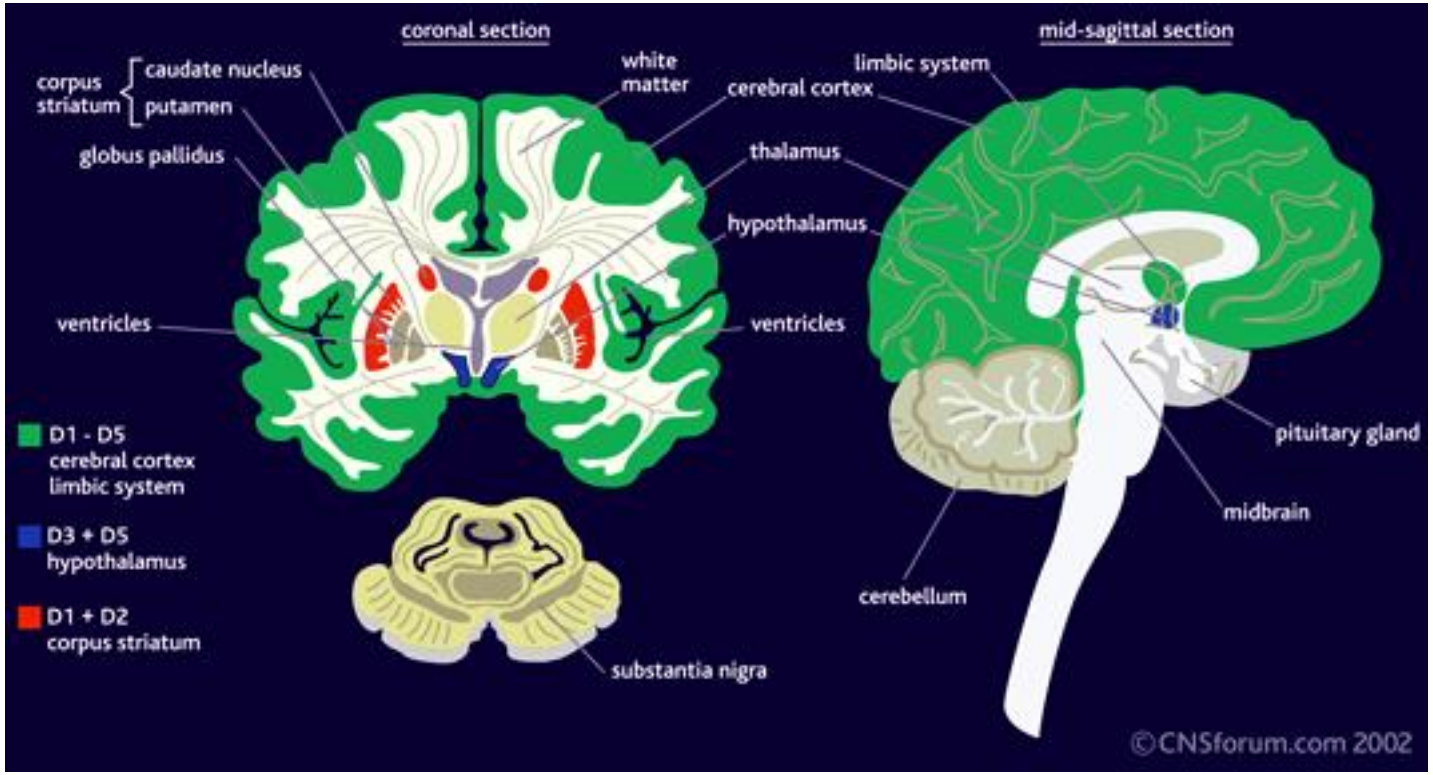
ACTION OF 5HT1A RECEPTOR ANTAGONIST



COURTESY OF LUNDBECK INSTITUTE, DENMARK

DOPAMINE RECEPTOR	
ATTRIBUTE	DESCRIPTION
NAME	DOPAMINE RECEPTOR
STRUCTURE	7 TRANSMEMBRANE
SUBTYPES	D1-LIKE AND D2-LIKE FAMILIES D1-LIKE,: D1, D5 RECEPTORS D2 LIKE: D2, D3, D4 RECEPTORS
EXPRESSION TYPES	WIDE DISTRIBUTION IN THE BRAIN. DOMINANT IN STRIATUM, N. ACCUMBENS, CORTEX
LIGAND BINDING	TRANSMEMBRANE SEGMENTS
BASIC ROLE(S)	D1-LIKE FAMILY ACTIVATES ADENYLYL CYCLASE D2-LIKE FAMILY INHIBITS ADENYLYL CYCLASE
AGONISTS	ROPINIROLE , PRAMIPEXOLE
ANTAGONISTS	CLOZAPINE, RISPERIDONE, OLANZAPINE, QUETIAPINE
FUNCTIONAL ROLES	REGULATION OF CNS NETWORKS, CONTROLLING MOVEMENT, MOOD, ADDICTION
DISEASES	PARKINSON DISEASE, SCHIZOPHRENIA, ATTENTION-DEFICIT HYPERACTIVITY DISORDER

DISTRIBUTION OF D1-D5 RECEPTORS IN THE HUMAN



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ADRENERGIC RECEPTOR	
ATTRIBUTE	DESCRIPTION
NAME	ADRENERGIC RECEPTOR. BINDS BOTH ADRENALINE AND NORADRENALINE
STRUCTURE	7 TRANSMEMBRANE
SUBTYPES	3 FAMILIES, ALPHA 1, ALPHA 2 AND BETA. SUBCLASSES IN EACH FAMILY
EXPRESSION TYPES	WIDE DISTRIBUTION IN THE BRAIN, HYPOTHALAMUS, CEREBRAL CORTEX IN THE CNS, ALPHA2A AND BETA 1 RECEPTORS ARE THE MAIN ADRENERGIC RECEPTORS ALPHA2A RECEPTORS PERFORM AS AUTORECEPTORS
LIGAND BINDING	THE EXTRACELLULAR DOMAIN OF THE RECEPTOR
BASIC ROLE(S)	ALPHA-2 ADRENERGIC RECEPTOR DECREASE CYCLIC AMP BETA ADRENERGIC RECEPTORS INCREASE CYCLIC AMP
AGONISTS	ISOPROTERENOL (SPECIFIC FOR BETA)
ANTAGONISTS	PROPRANOLOL (BETA), PHENTOLAMINE (ALPHA, WITH SOME BETA ACTION)
FUNCTIONAL ROLES	REGULATION OF CNS AND PNS FUNCTIONS
DISEASES	ANXIETY, POSTTRAUMATIC STRESS DISORDER (PTSD)