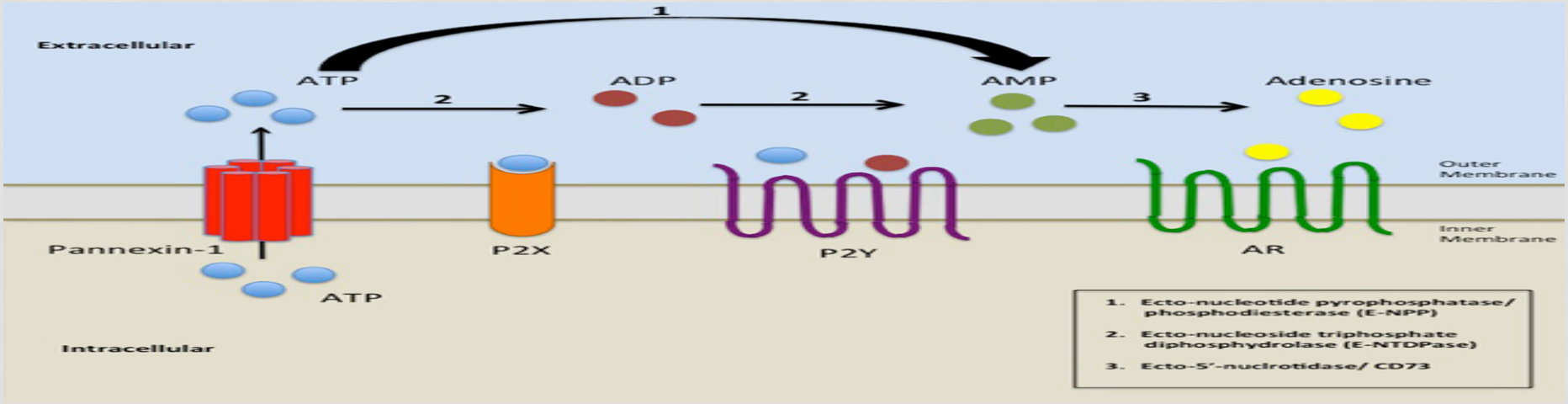

PURINERGIC RECEPTOR

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ASSISTANT PROFESSOR, RIPS, BERHAMPUR

HISTORY

- **The transmitter substance release from Non-cholinergic & Non-adrenergic nerves of Gut may be ATP or some related purine nucleotide.**

- **These nerves has been termed as “Purinergic nerves”**

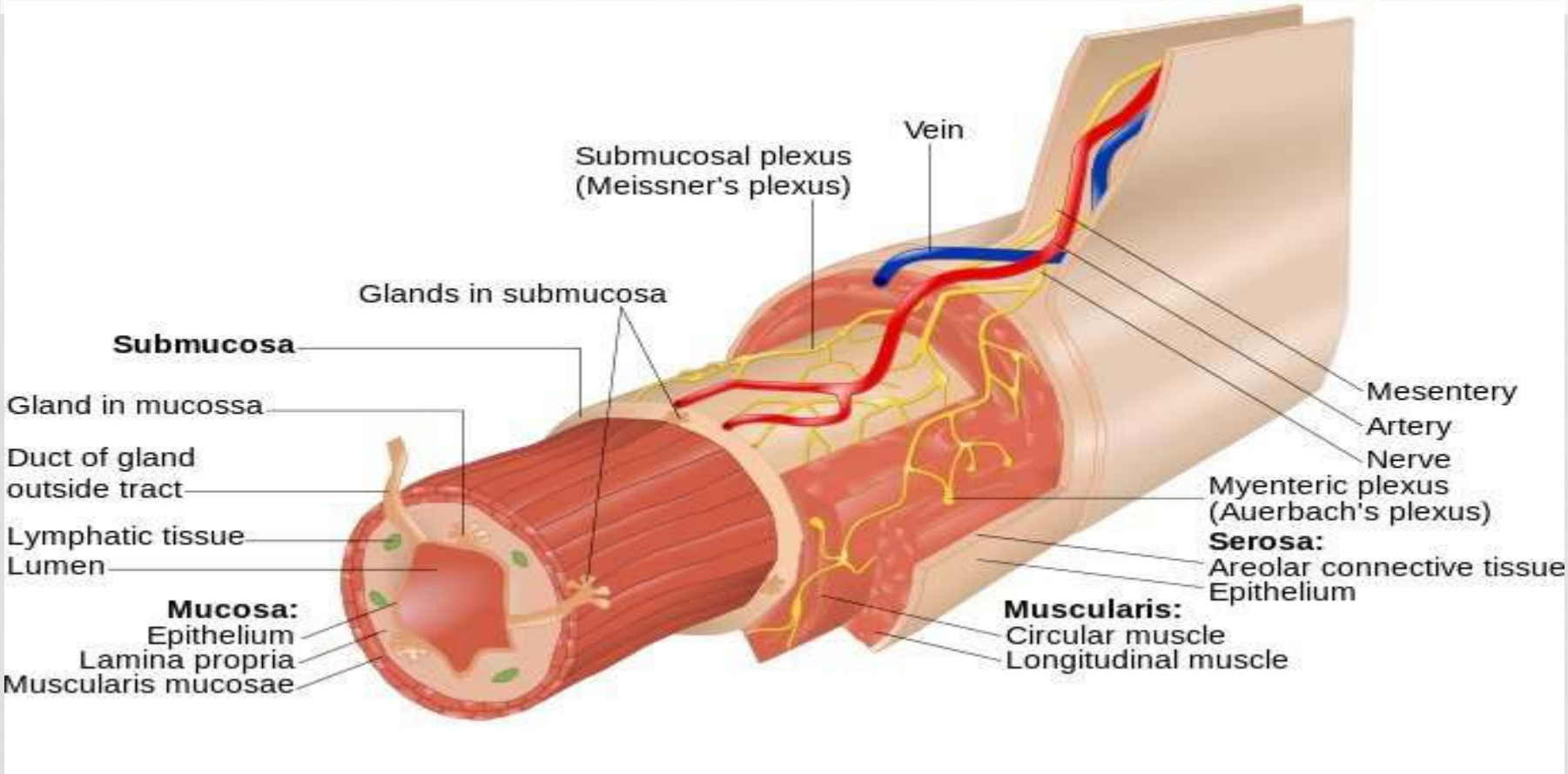
INTRODUCTION

What is purinergic receptors?

- **The purinergic system involves the purine nucleotides, ATP , ADP, and the nucleoside adenosine.**

- **Purinergic nerves are located on Aurbach's plexus.**

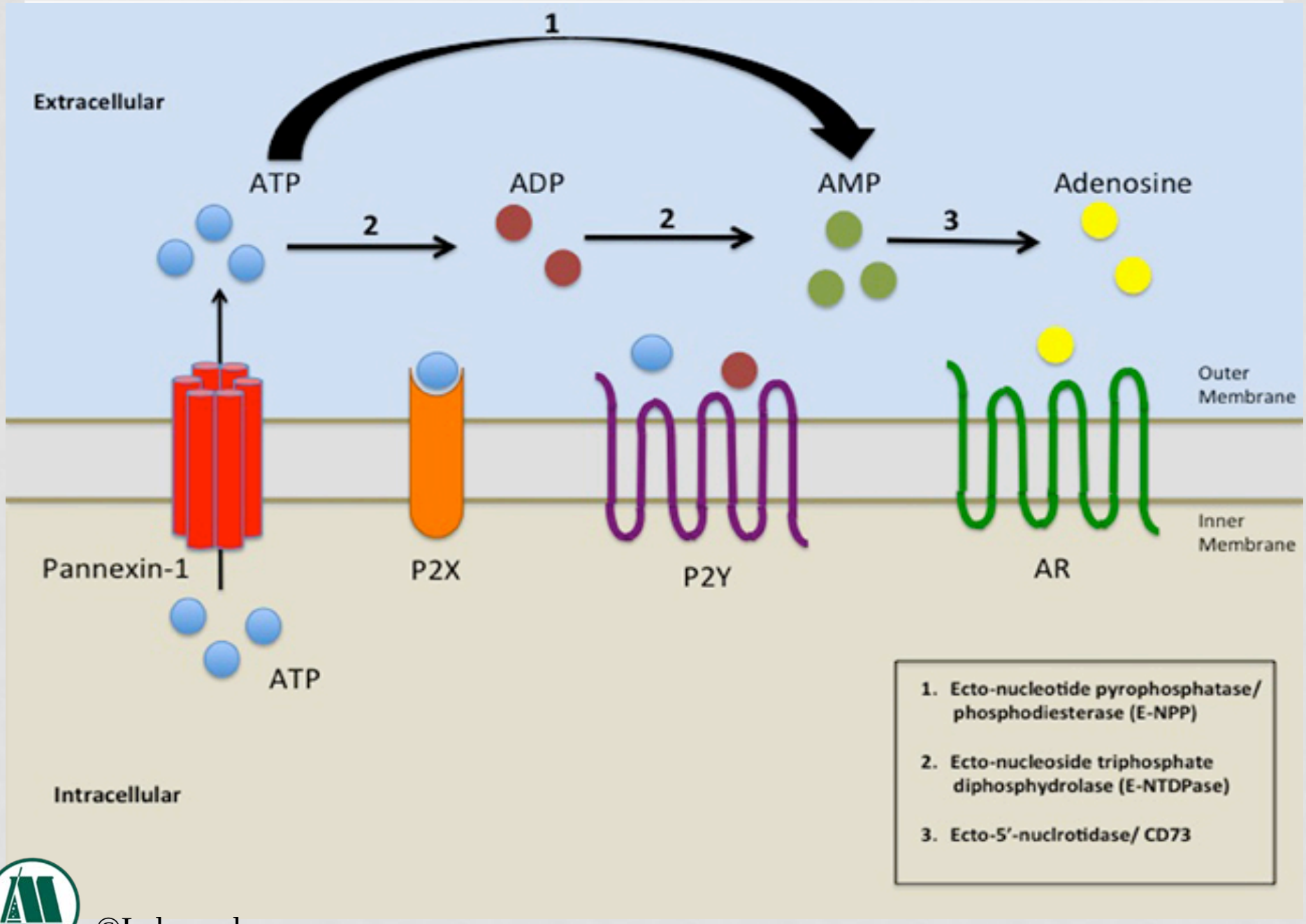
AURBACH'S PLEXUS



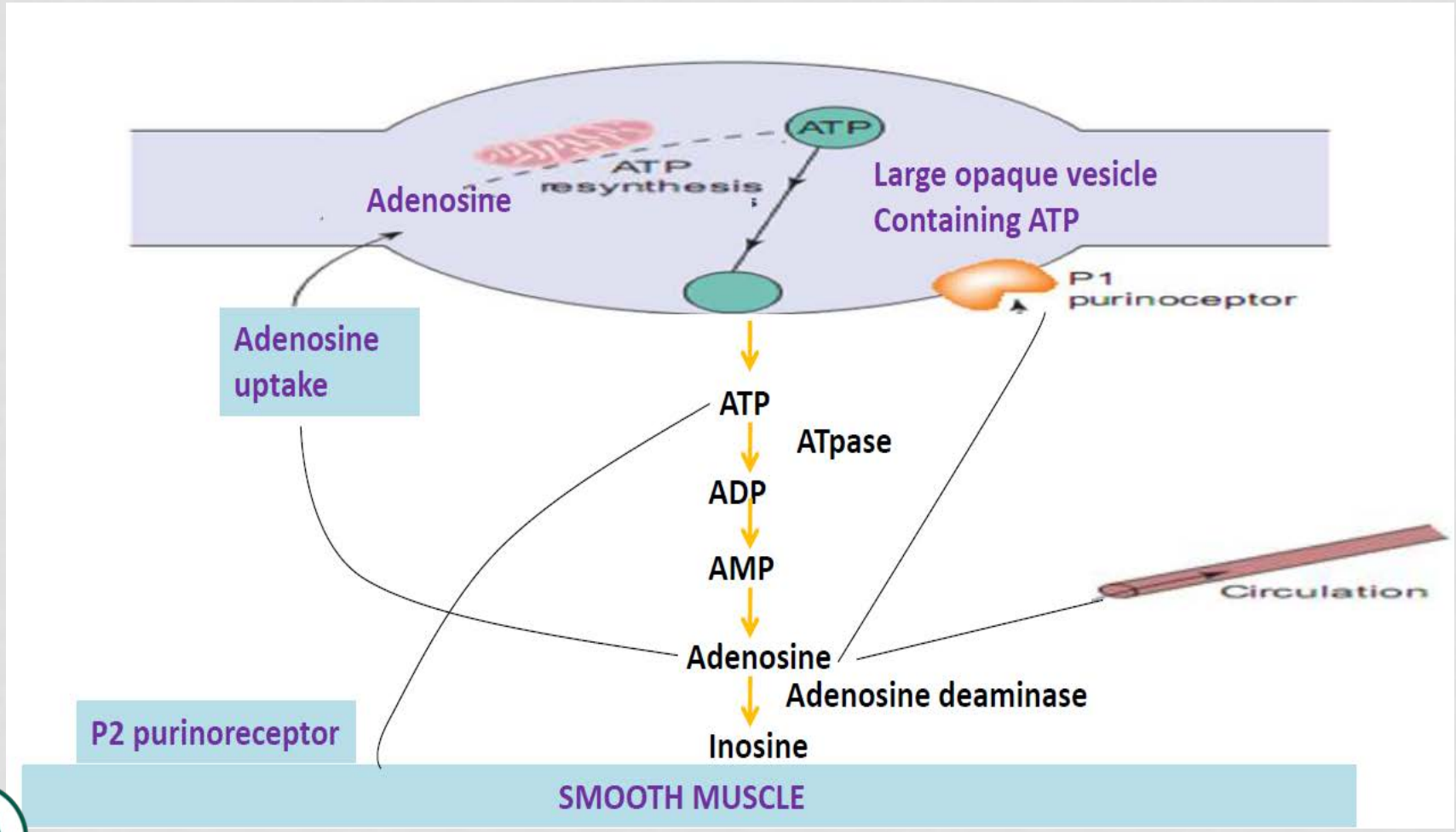
- Aurbach's plexus is a collection of nerve fibre and that are mainly found in the muscle tissue of human intestine .
- These plexus are mainly responsible for generating peristalsis movement.

ATP AS A NEUROTRANSMITTER

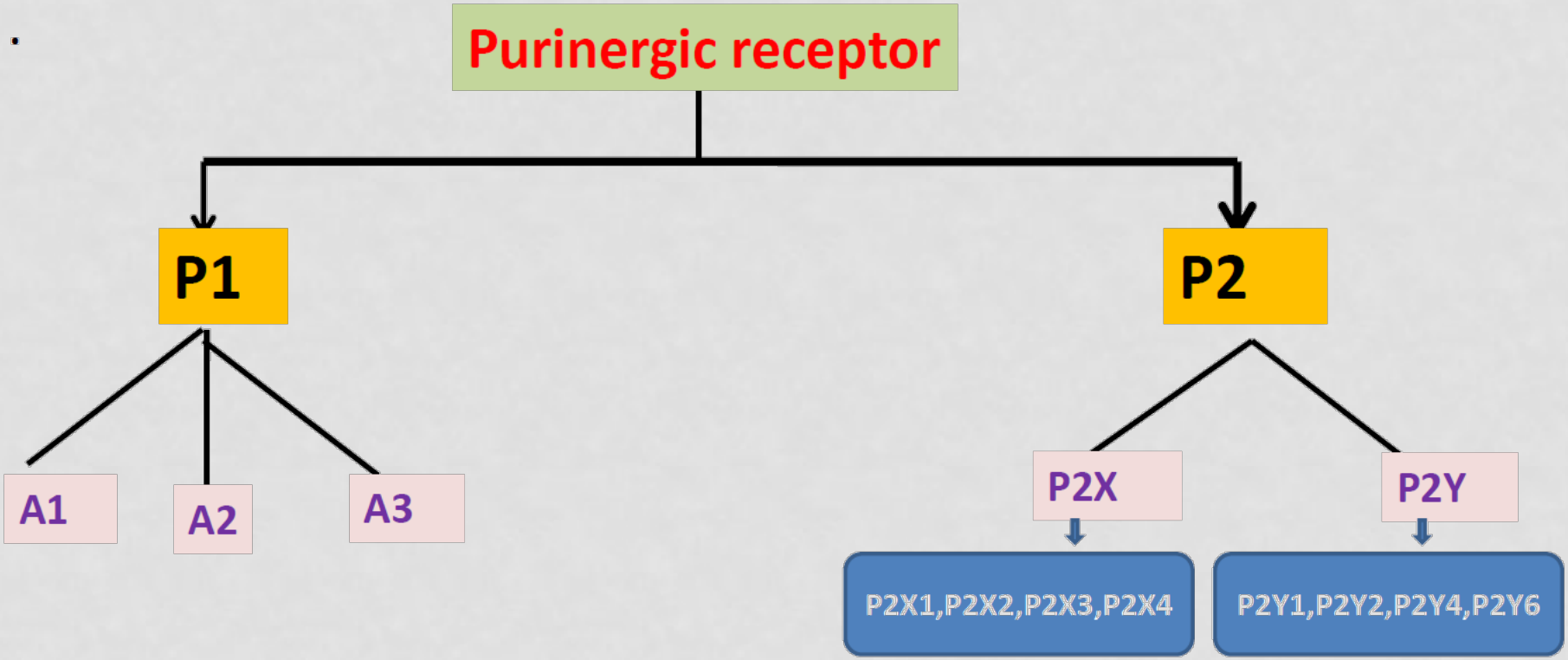
- **The substance must be released from terminal axon when nerves are activated.**
- **ATP is contained in synaptic vesicles of both adrenergic and cholinergic neurons, and it works as an energy currency.**
- **ATP is released on nerve stimulation in a Ca2+-dependent fashion**


1
Extracellular
ATP
ADP
AMP
Adenosine
2
2
3
Outer Membrane
Inner Membrane
Pannexin-1
P2X
P2Y
AR
ATP
Intracellular
1. Ecto-nucleotide pyrophosphatase/ phosphodiesterase (E-NPP)
2. Ecto-nucleoside triphosphate diphosphydrolase (E-NTDPase)
3. Ecto-5'-nuclrotidase/ CD73

SYNTHESIS, STORAGE, RELEASE AND METABOLISM OF ATP



TYPES OF PURINERGIC RECEPTORS



DISTRIBUTION OF PURINERGIC RECEPTORS

Receptors	Main distribution
A1	Brain, spinal cord,testis,heart.
A2	Brain, Heart,spleen, lungs.
A3	Lung,Liver, Brain, Testis.

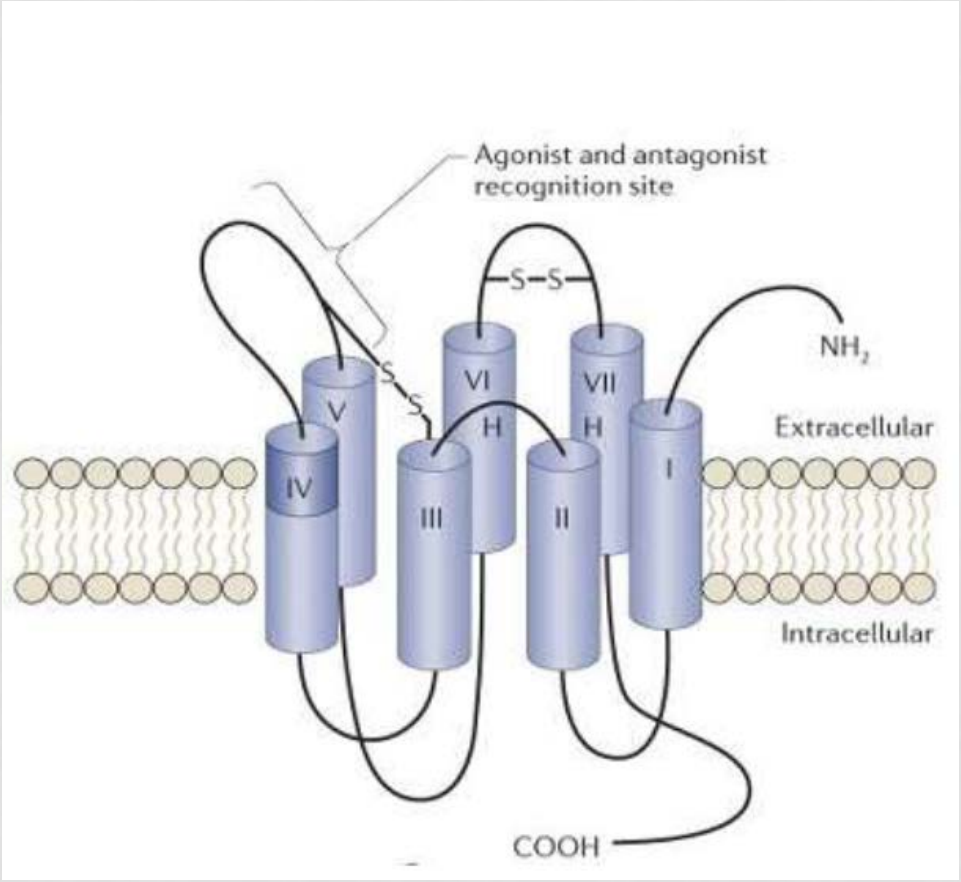
Receptors	Main distribution
P2X1	Smooth muscle, cerebellum, platelets
P2X2	Smooth muscle, sensory, gangalia
P2X3	Sympathetic neurons
P2X4	CNS, testis,colon

Receptors	Main distribution
P2 Y1	Epithelial cell,Endothelial cell,
P2Y2	Immun cell, osteoblast,kidney tubules
P2Y4	Endothelial cell
P2Y6	Placenta,T cell,thymus

STRUCTURE OF PURINE RECEPTOR

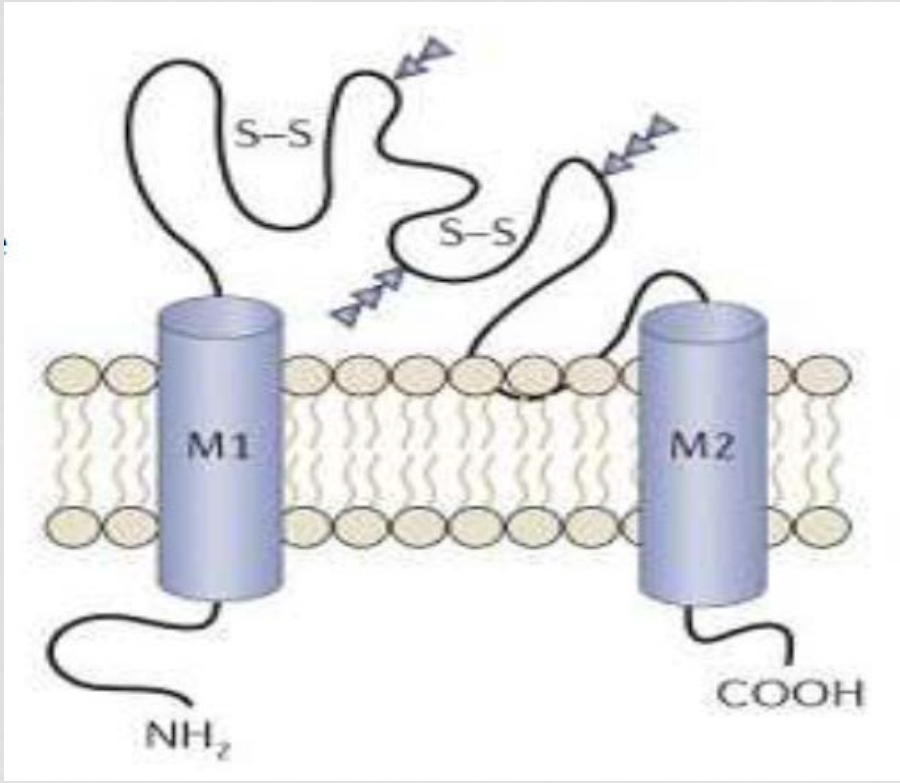
- P1 receptor:- (G- protein couple receptors)

7-Transmembrane(TM) domains of hydrophobic amino acid--- constitute an α-helix of ~21–28 amino acids



STRUCTURE OF PURINE RECEPTOR

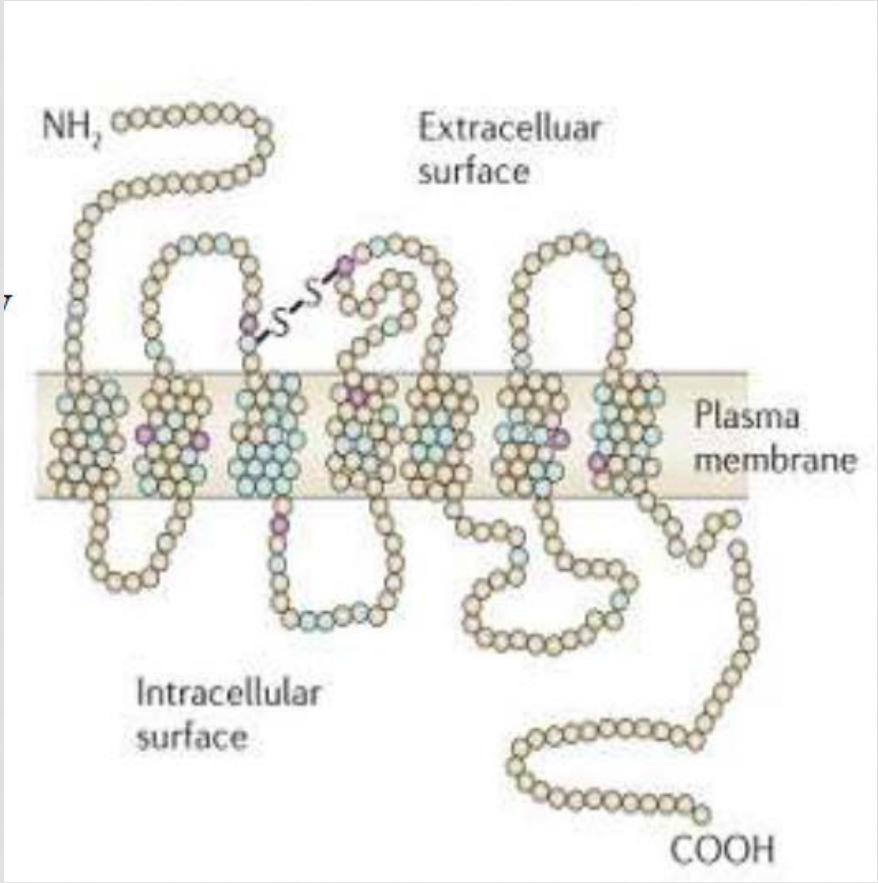
- P2x receptor :- (Ligand gated ion channel)
- Large extracellular loop, with 10 conserved cysteine residues forming a series of disulfide bridges.



STRUCTURE OF PURINE RECEPTOR

- **P2y receptor :-(G- protein couple receptor)**

Some TM-spanning regions, particularly TM3, TM6 & TM7 and structural diversity of intracellular NH2 & COOH terminus among P2Y sub-Types

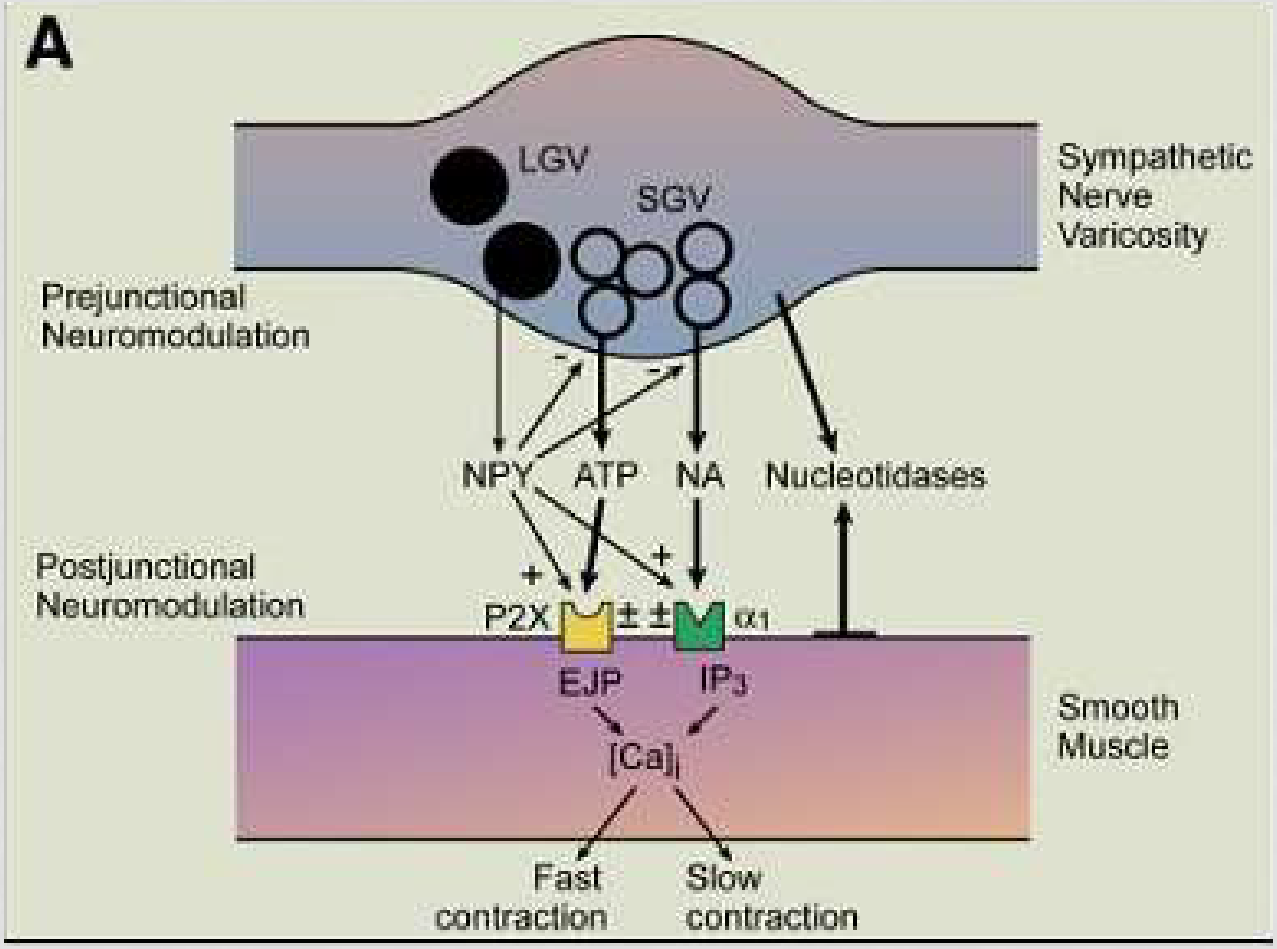


PURINERGIC SIGNALLING

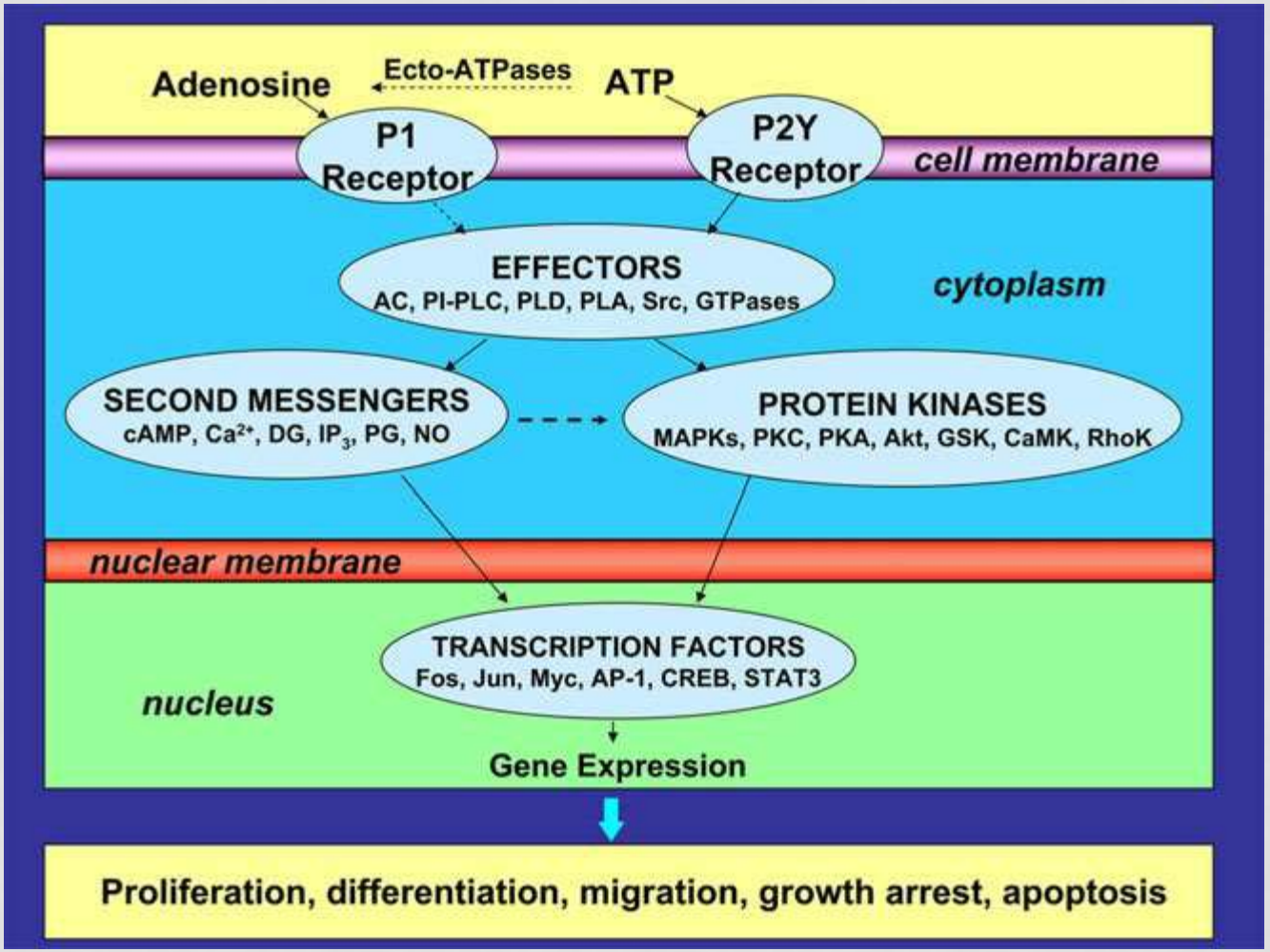
- **Short term neuronal signalling-**
- **secretion**
- **vasodilation**
- **Co-transmission**

- **Long term neuronal signalling**
- **Cell proliferation**
- **Cell differentiation**
- **Inflammation**

CO-TRANSMISSION



CELL PROLIFERATION AND DIFFERENTIATION



ROLE OF PURINERGIC RECEPTOR

- 1) In Central Nervous System
- 2) In Respiratory System
- 3) In Cardiovascular System
- 4) In Gastrointestinal Tract
- 5) In endocrine system
- 6) In Urinary system

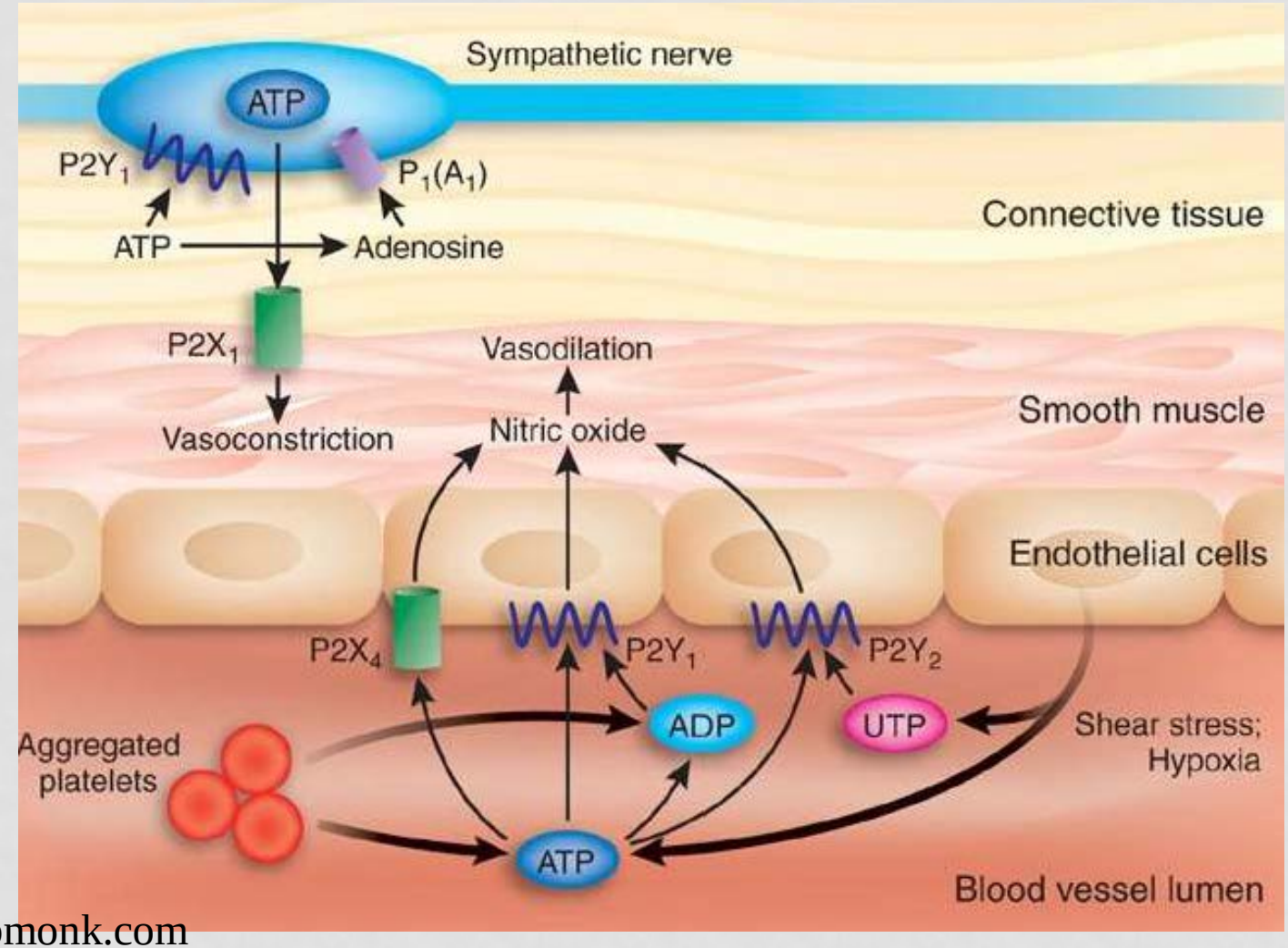
CENTRAL NERVOUS SYSTEM

- Release of excitatory neurotransmitter (GABA, glycine)
- Release of inhibitory neurotransmitter (glutamate)
- Anticonvulsant effects

RESPIRATORY SYSTEM

- Purine increases mucus secretion from goblets cells.
- Purinergic activation causes bronchoconstriction.

CARDIAC SYSTEM



IT CAUSES

- Slows AV nodal conduction (negative dromotropy)
- Decrease heart rate (negative chronotrophy)
- Decrease atrial contractility (negative contraction)
- Inhibits pacemaker

GASTROINTESTINAL TRACT

- Relaxation of stomach.
- Decreases peristalsis movement.
- P2x3 receptor present on gut wall produces pain sensation

URINARY SYSTEM

- Purinergic signaling causes contraction of urinary bladder.
- Purinoceptor involved in regulation of renin secretion, glomerular filtration and transport of water, ions, nutrients.
- P2x3 responsible for micturation reflux and pain

ENDOCRINE GLANDS

- ATP stimulate release of insulin
- ATP modulate aldosterone production
- ATP inhibit secretion of estradiol and progesterone from ovary
- Inhibit lipolysis

THERAPEUTIC POTENTIAL

- 1) **Parkinson's disease :-**
- Adenosine A2a receptor antagonists are mainly used.

- 2) **Epilepsy :-**
- Adenosine by activation of A1 receptors in hippocampus exerts predominant inhibitory effects.
- These inhibitory actions of adenosine can be used therapeutically to suppress seizures.

3) **Ischemia :-**

Adenosine used as a cytoprotective agent during myocardial ischemia

i) improved tissue perfusion ii) anti-inflammatory action

THERAPEUTIC POTENTIAL

- **Atherosclerosis:-**

Adenosine and ATP have a number of cardiovascular protective effect in addition of vasodilation ,including promotion of the endothelial and smooth muscle cell proliferation and increased in the expression of vascular endothelial growth factor (VEGF).

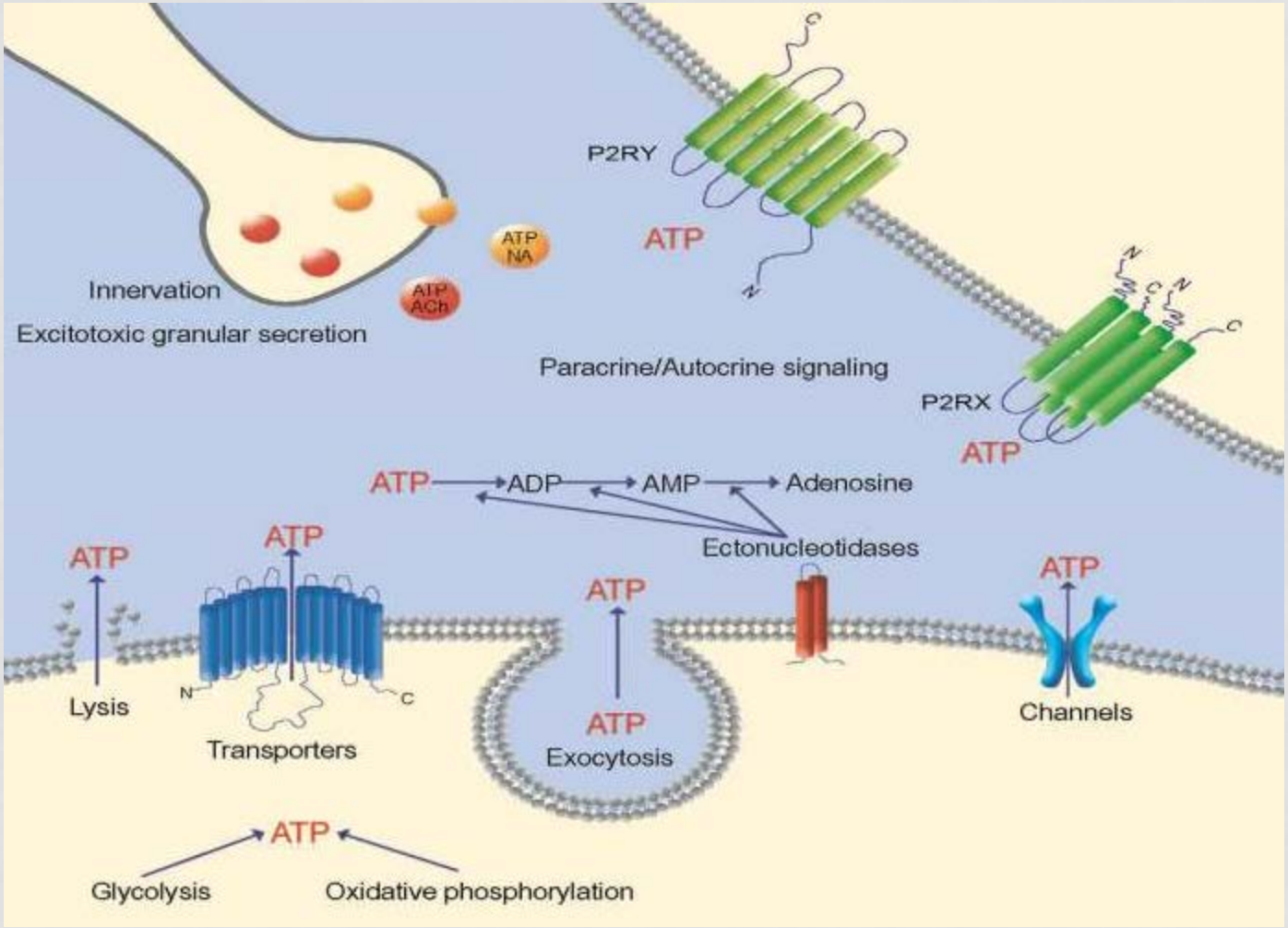
RECENT TRENDS

- **Purinergic signalling in ovary**
- **Acupuncture : a Novel hypothesis for involvement of purinergic signaling**

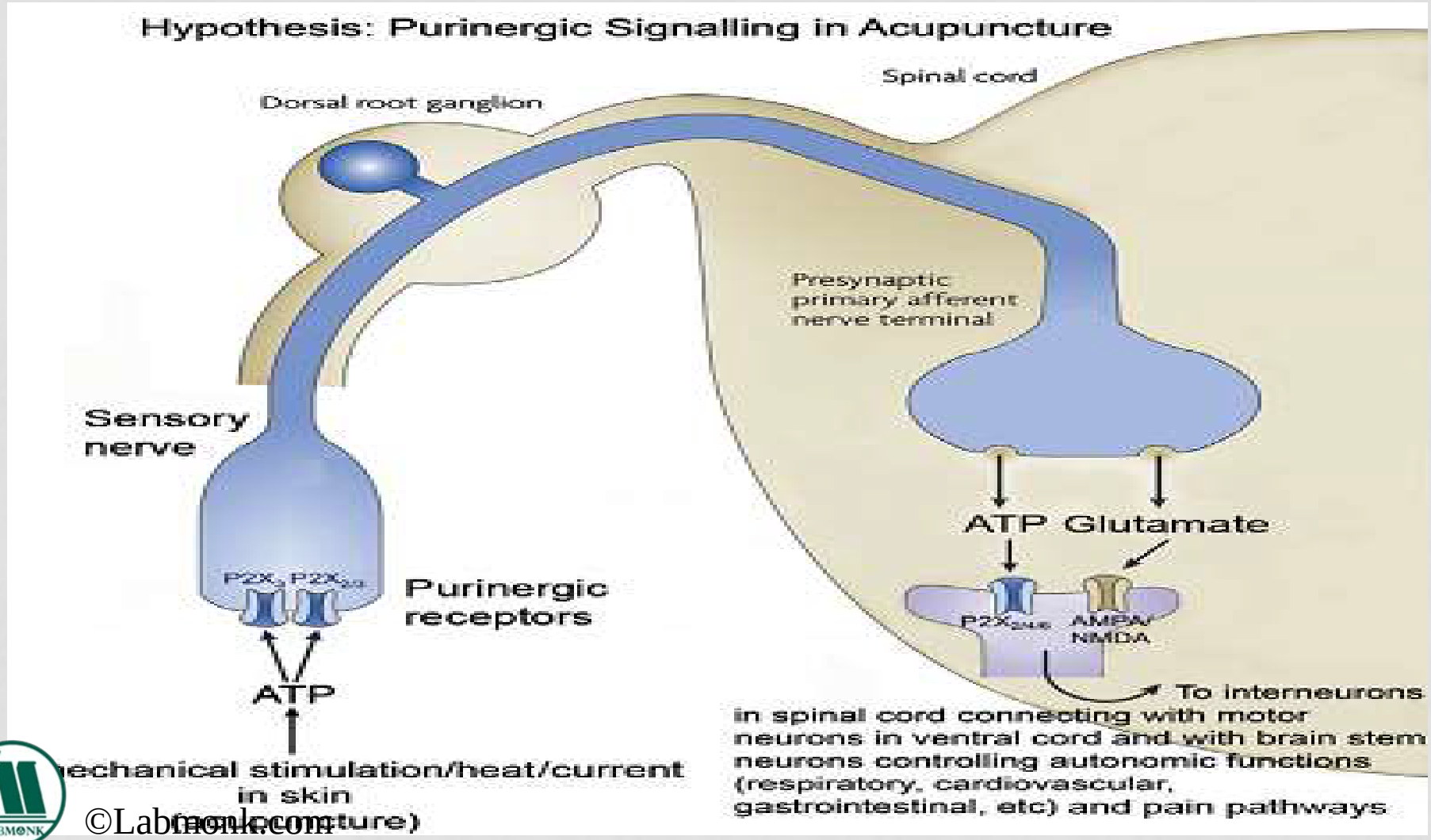
PURINERGIC SIGNALLING IN OVARY

- ATP produced inside the cell can be released into the extracellular area in different ways.
- purinergic activity in ovary – including sensitivity of gonadotropin in several ovarian cells types, i.e Granulosa cell , theca cell.
- role of ATP as an important intra-ovarian messenger and regulate the ovarian function.

SIGNALLING IN OVARY



ACUPUNCTURE: A NOVEL HYPOTHESIS FOR THE INVOLVEMENT OF PURINERGIC SIGNALLING



THANK YOU

FOR LISTINING PATIENTLY……