Cell signaling is the process of cellular communication within the body driven by cells releasing and receiving hormones and other signaling molecules. As a process, cell signaling refers to a vast network of communication between, and within, each cell of our body. Cell signaling enables coordination within multicellular organisms.

Cell signaling can occur through a number of different pathways, but the overall theme is that the actions of one cell influence the function of another. **Cell signaling is needed by multicellular organisms to coordinate a wide variety of functions.**

1) Communication between cells
2) Communication between cells which regulate and modulate cellular function
3) It installed a signaling pathway between target cell and signaling producing cells
4) It occurs in prokaryotes and eukaryotes.

For examples-

a) Nerve cells must communicate with muscle cells to create movement,
b) Immune cells must avoid destroying cells of the body.
c) Cells must organize during the development of a baby.

Signaling cascades-

Cell require a full functional machinery of life, it belongs to simple to complex, multicellular organism. Cell requires communication with other cells to work for symbiosis for providing the proper life of organism. This communication between

Stages of Cell Signaling- its core cell signaling can simply be described as the production of a signal by one cell. This signal is then received by a target cell. In effect, signal transduction is said to have three stages:

- First, reception, whereby the signal molecules binds the receptor.
- Then, signal transduction, which is where the chemical signal results in a series of enzyme activations.
- Finally, the response, which is the resulting cellular responses.

Important terms are used in signaling pathway.

Induction- Interaction of two or more cells or tissues of different history and properties is called proximate interaction or induction. Two main component shows inductive interaction.

1. **Inducer-** Tissue produced a signal that changes cellular behavior of the other tissues.
2. **Responder-** Second component, the tissues being induced is known as responder

Types of Cell Signalling Molecules- Cell signalling molecules are of the following types:

- **Intracrine ligands:** These are produced by the target cell and bind to the receptor within the cell.
- **Autocrine ligands:** They function internally and on other target cells. For eg., immune cells.
- **Juxtacrine ligand:** These target the adjacent cells.
- **Paracrine ligands:** These target the cells in the vicinity of the original cells. For eg., neurotransmitters
- **Endocrine ligands:** These produce hormones.

Stages of Cell Signalling- Cell signalling takes place in the following three stages:

- Binding of the signal molecule to the receptor.
- Signal transduction, where the chemical signals activate the enzymes.
- Finally, the response is observed

Cell Signalling Pathways- The cell signalling pathways are either mechanical or biochemical. The cell signalling is categorized based on the distance it must travel. For instance, hydrophobic ligands include steroids and vitamin D3. These can diffuse across the plasma membrane of target cells and bind to the intracellular cells. On the contrary, hydrophilic ligands bind to the receptors on the surface of the cell and are amino acid-derived. These allow the signals to pass through the aqueous environment of our body without any assistance.

Cell Signalling Function

•Intracellular Receptors. **Intracellular receptors are common types of cell signalling receptor located within the cell in the cytoplasm. The intracellular receptors are of two types:Cytoplasmic receptors**- cell signalling receptor located within the cell in the cytoplasm, they bind or phophorylated and induced function.

•Nuclear receptors- Nuclear receptors are special classes of proteins with diverse DNA binding domains that form a complex with thyroid hormones that enter the nucleus and regulate the transcription of a gene.

•**Ligand Gated Ion Channels**- These allow hydrophilic ions to pass the plasma membrane. When a neurotransmitter such as acetylcholine binds to it, ions cross the membrane and allow the neural firing to take place.

•G**-Protein Coupled Receptors**- These receptors receive a large number of signals from diverse groups. The mechanism of action starts when a ligand binds to the receptor. This activates the G-protein that transmits an entire cascade of enzymes. It also activates the second messengers that carry out several functions such as sight, inflammation, growth and sensation.

•**Tyrosine Kinase-** A ligand binds to the receptor tyrosine kinase that results in the dimerization of the kinase domains. The tyrosine kinase domains of the dimer then phosphorylate that allows the intracellular proteins to bind the phosphorylated sites and activate.

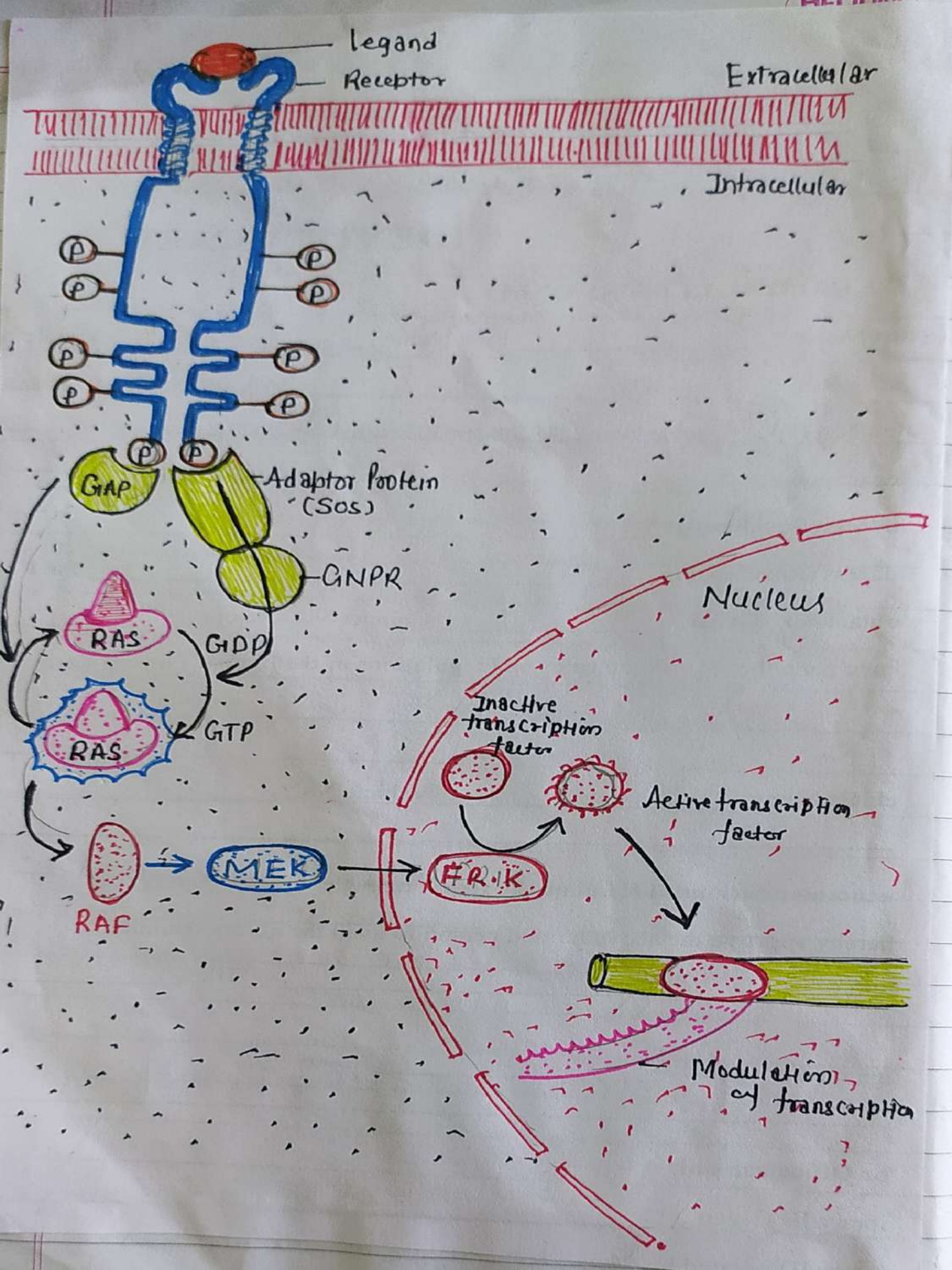
Legands = Paracrine factor

Several types Signal transduction pathway have been discovered. Each receptor binds (spans) with cell membrane.

(1) Extracellular region
(2) Transmembrane region
(3) Cytoplasmic region

R.T.K. Receptor ~~Kinase~~ Tyrosine Kinase

(1) It play important role in regulations of cell growth, differentiation and survival. In other words we can say it control and regulate cell growth
(2) If R.T.K. do not function properly it causes Cancer


legand
Receptor
Extracellular
Intracellular
P
GAP
Adaptor Protein
(Sos)
GNPR
RAS
GDP
GTP
RAS
RAF
MEK
FRK
Nucleus
Inactive transcription factor
Active transcription factor
Modulation of transcription

R.T.K. Signal Pathway

1. It is one of the 1st pathway to unite various areas of development biology
At cell surface, RTK bind with legands
R.T.K spans the cell membrane and when it binds with legands
Binding of the legand to the receptor cause the autophosphorylation of the cytoplasmic domain of the receptor

↓

The phosphorylated tyrosin on the receptor is then recognised by an adaptor protein

↓

In cytoplasmic domain also activate G. protein normal G protein is inactive

↓

When (G) it bounds adaptor protein it become GNRPC (Guanine Nucleotide releasing factor)

↓

GNRP exchange a phosphate form a GTP to transform GDP in GTP

↓

GTP bond G protein is an active form that transmit the signal

↓

G protein bounds with GDP is known as RAS

After delivering the signal GTP of G protein is hydrolyzed back into GDP. This catalysed greatly stimulated by GAP (GTPase activating protein)

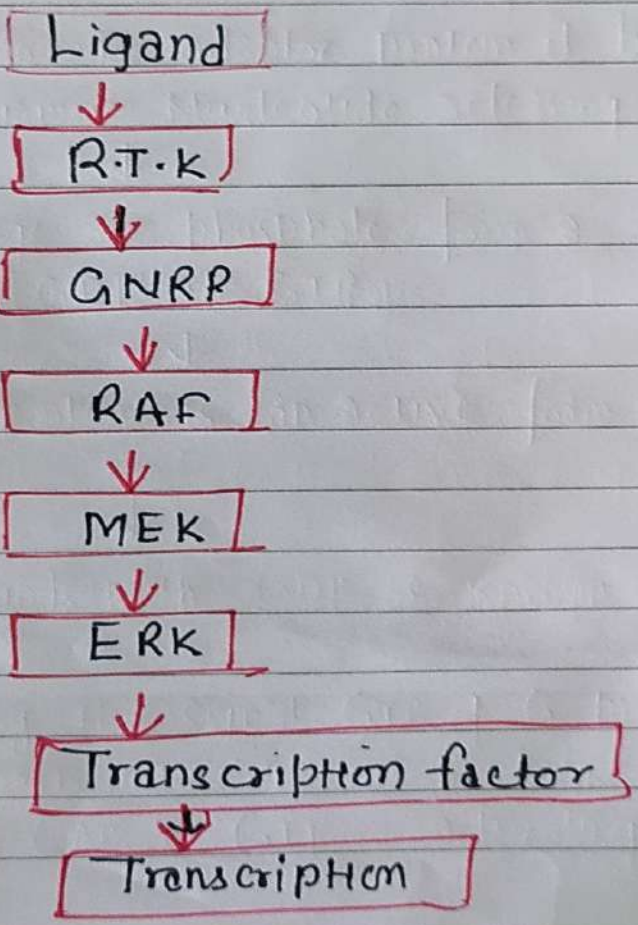
In this G protein return to its inactive state where it can await further signaling.

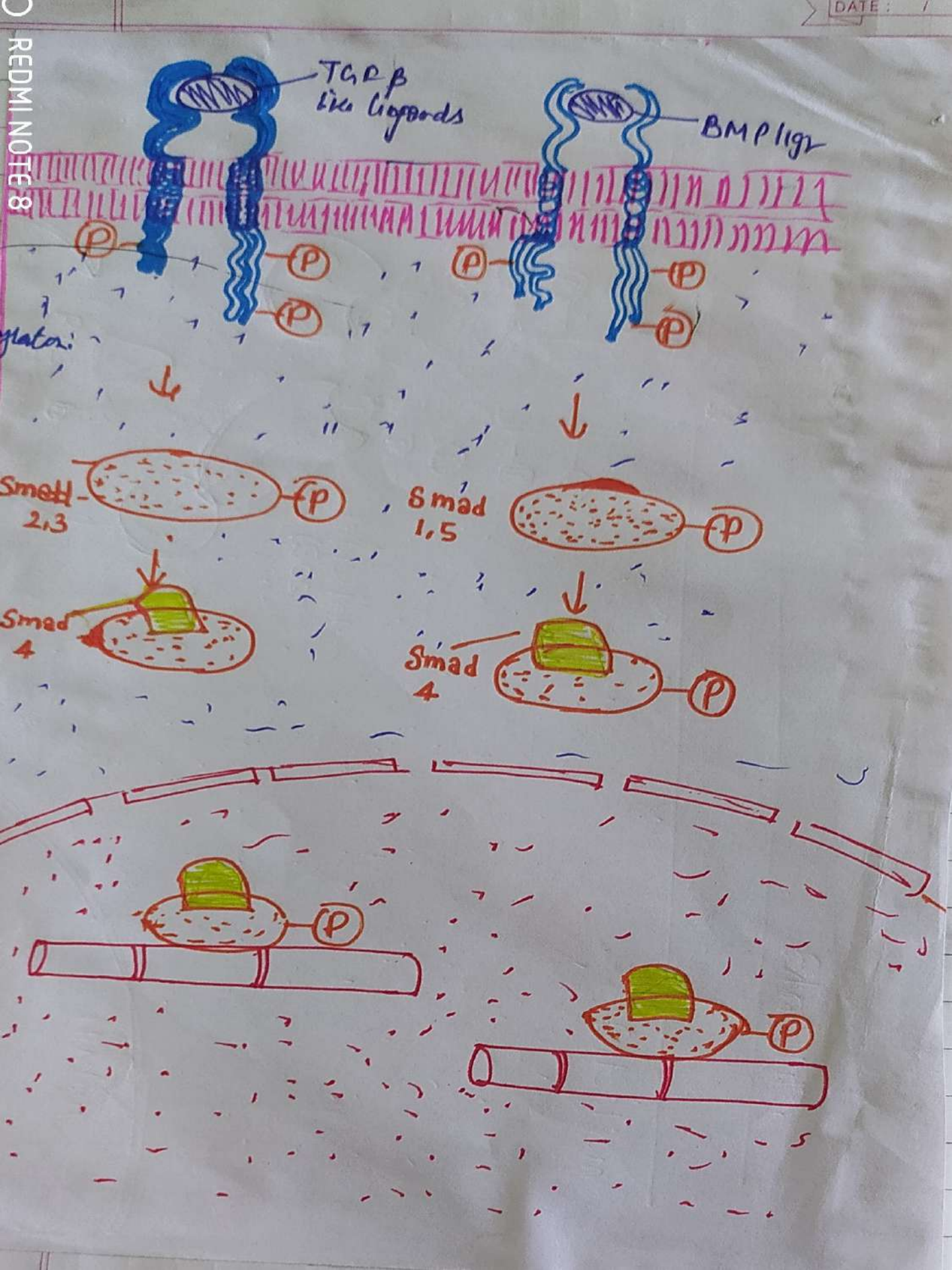
Active G protein associated with a kinase called RAF. RAF is inactive protein to the cell membrane it become active

Active form of RAF is a kinase it activate the MEK protein by phosphorylation

MEK itself kinase, which activate ERK, ERK enter in the nucleus

In nucleus it phosphorylate certain transcription factor




TGF β
like Ligands
BMP ligs
P
Smad
2,3
Smad
1,5
Smad
4
Smad
4

Wnt Pathway

It is regulate cell fate determination, cell migration cell polarity, neural patterning and organogenesis during embryogenesis or embryogenic development.

1. Members of Wnt pathway family of paracrine factors interact with frizzled family

Q. Binding of Wnt and frizzled protein activate Disheveled protein

When Disheveled protein is activated it inhibit the activity of GSK-3 (Glycogen synthase kinase) it degrade the β- catenin for dissociation

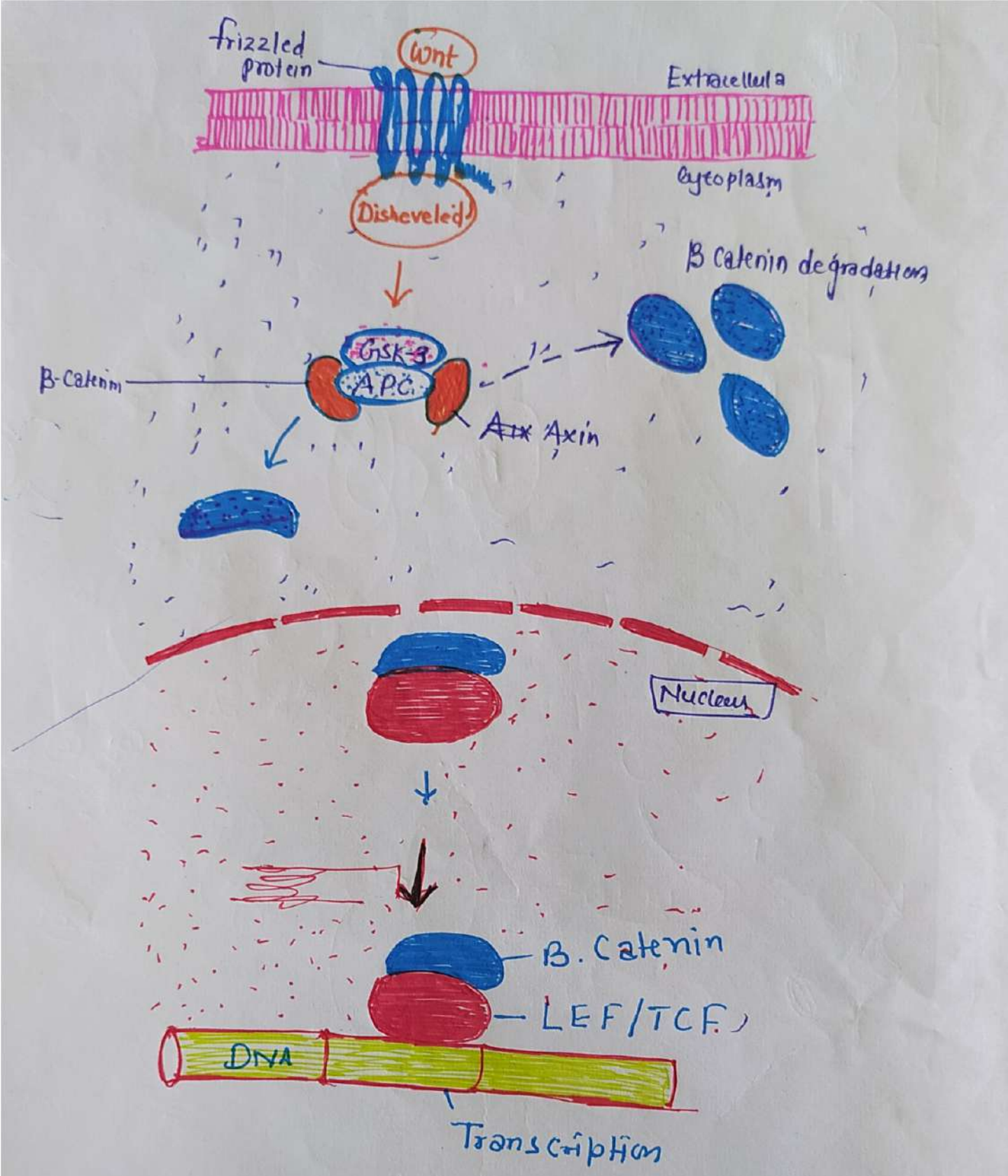
When GSK inhibit, β catenin can dissociate from APC protein and enter nucleus

β- Catenin in nucleus form hetero dimer LEF and TCF DNA binding protein

↓

Start transcription

Wnt → frizzled → Dischevelled → GSK-3 → β catenin → Transcription


frizzled protein
Wnt
Extracellular
Cytoplasm
Dishevelled
B catenin degradation
GSK-3
A.P.C.
B-Catenin
Axin
Nucleus
B. Catenin
LEF/TCF
DNA
Transcription

Wnt - Pathway

The hedgehog Pathway

Hedgehog protein binding the receptor ~~to a~~ called patched protein

Patched protein is not a signal transducer, it is bound to signal transducer called smoothen protein

Patched protein prevents the smoothened protein from functioning

In the absence Hedgehog binding to patched, Smoothen protein is inactive

↓

While its microtubule is cleaved the CI

↓

Cleaved CI inter in the nucleus and act as a transcription repressor

↓

When hedghoge binds to patched protein by phosphorylation

↓

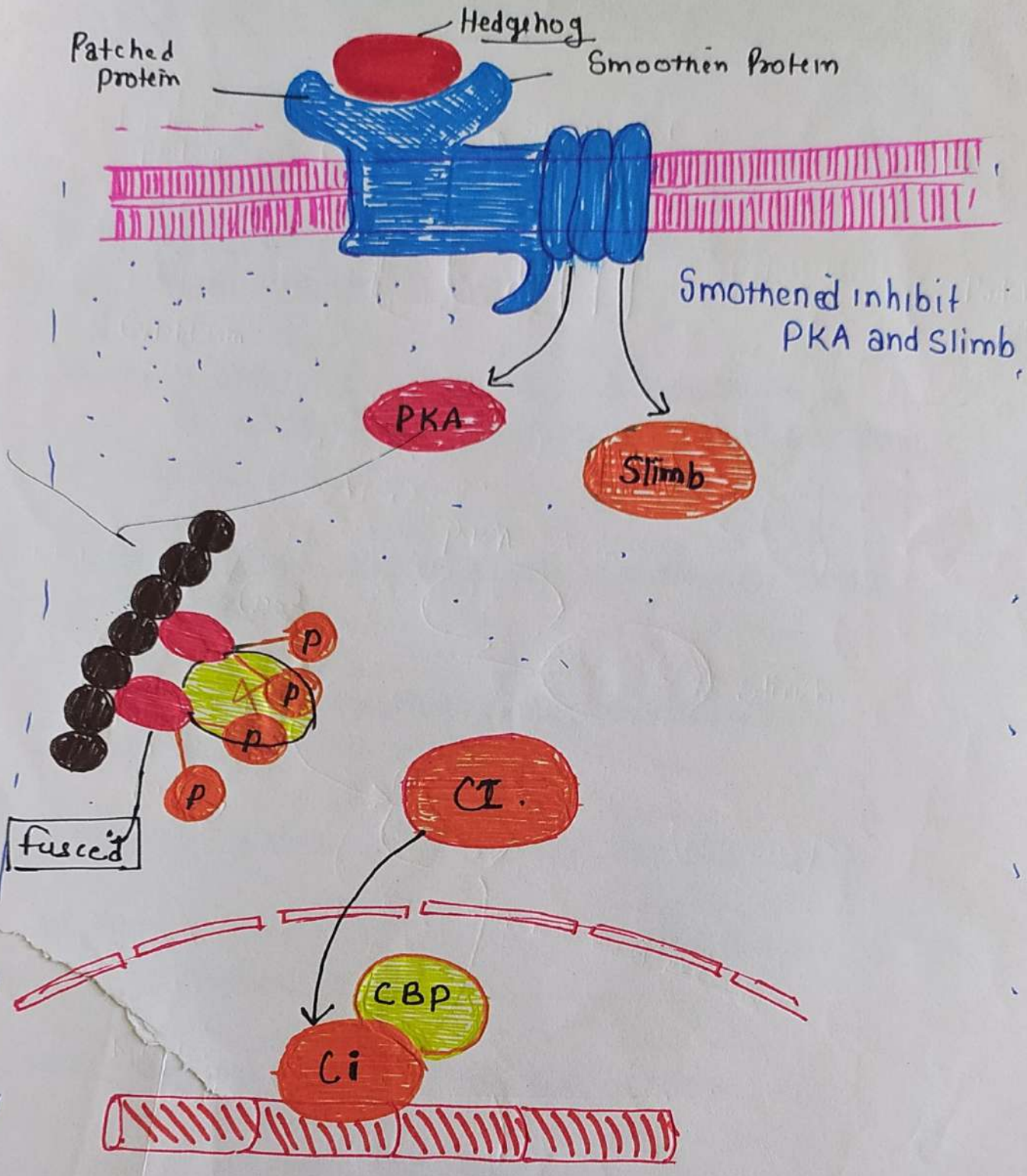
Smoothen protein release the CI protein to microtubule

↓

CI Enter nucleus

↓

It works in nucleus as transcription activator.



Transcription of hedgehog response protein

Notch Pathway.

Important Signaling System in multicellular organism in development and homeostasis

1. It regulate - cell proliferations
2. cell fate
3. cell differentiation
4. Apoptosis
5. Neural development in embryogenasis
6. It involve in development in sensory hairs
7. it is Single pass transmembrane protein
8. Iell induce the messagi by Ca^{++}, which released by E.R.

1 Cells expressing Delta, Jagged or Serrate protein in their cell membrane, activate neighbouring cell, that contain notch protein in their cell membrane.

2. ↓

(2) Notch extend through cell membrane and its external surface contact to Delta, Jagged or Serrate proteins

↓

(3) It forms the complexed to one of their legand

↓

(4) Notch undergo a conformational changes that enable it to be Cut by a protease.

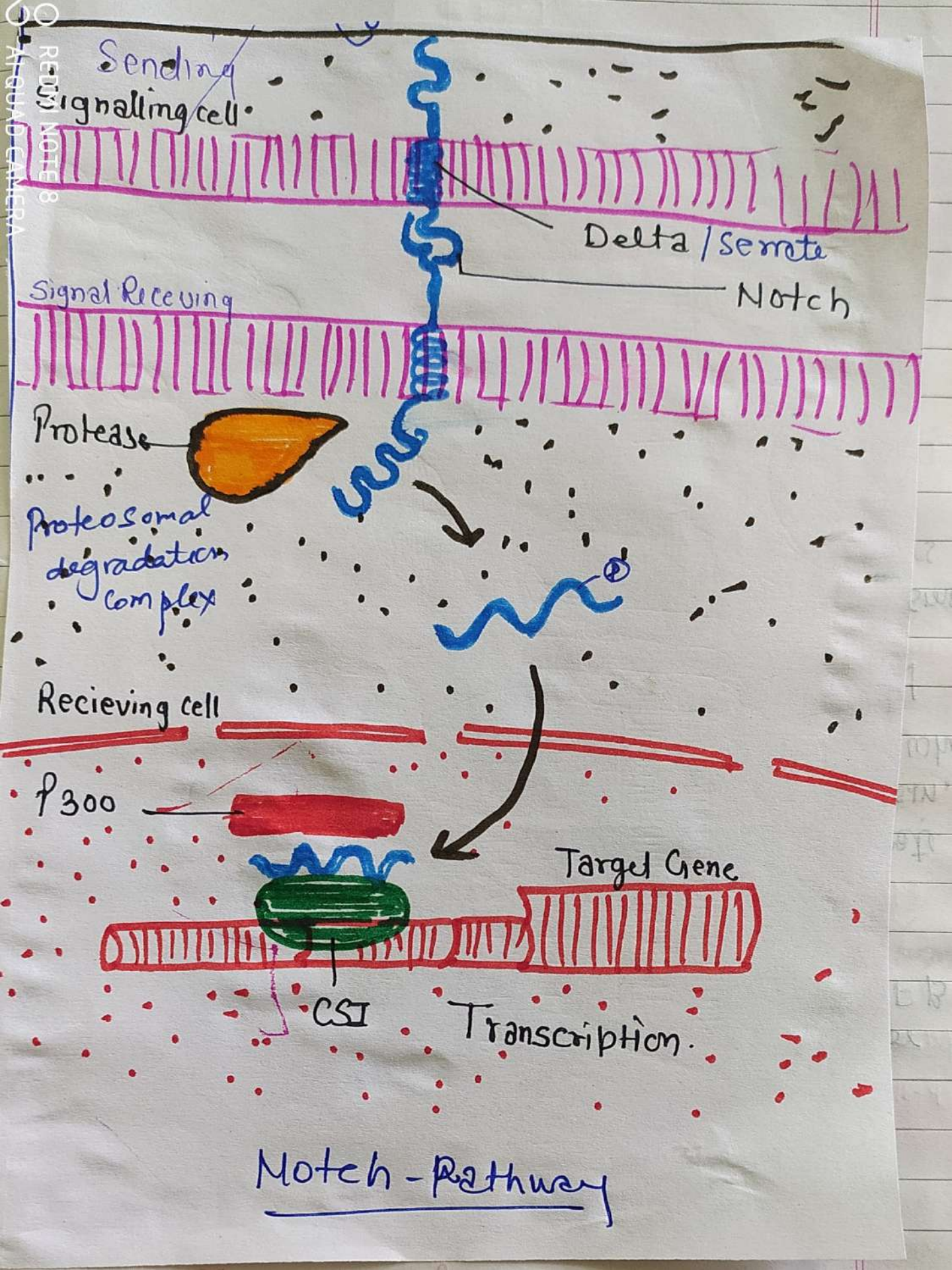
↓

Cleave portion of notch @ enter in the nucleus and bind to a dormant factor of C.S.L family

Dormant CSL factor after binding become activate

↓

Activate CSL start transcription.



Notch - Pathway

Interaction of protein in a cell.

It involve in immunity, cell division, cell death and tumour formation

Disrupted JAK STAT signalling may lead to a variety of disease such as cancer, immunity effect etc.

The endocrine factor prolactin binds to the extracellular regions of prolactin receptor

↓

Them to dimorize

↓

JAK proteins brough to gether

↓

phosphorylate several sites

↓

Now JAK proteins are activated

↓

JAK can have their protein kinase activity

↓

Activated receptor can now phusphorylate particular inactive STAT

↓

Cause dimerize STAT

↓

STAT become activated after dimerization

↓

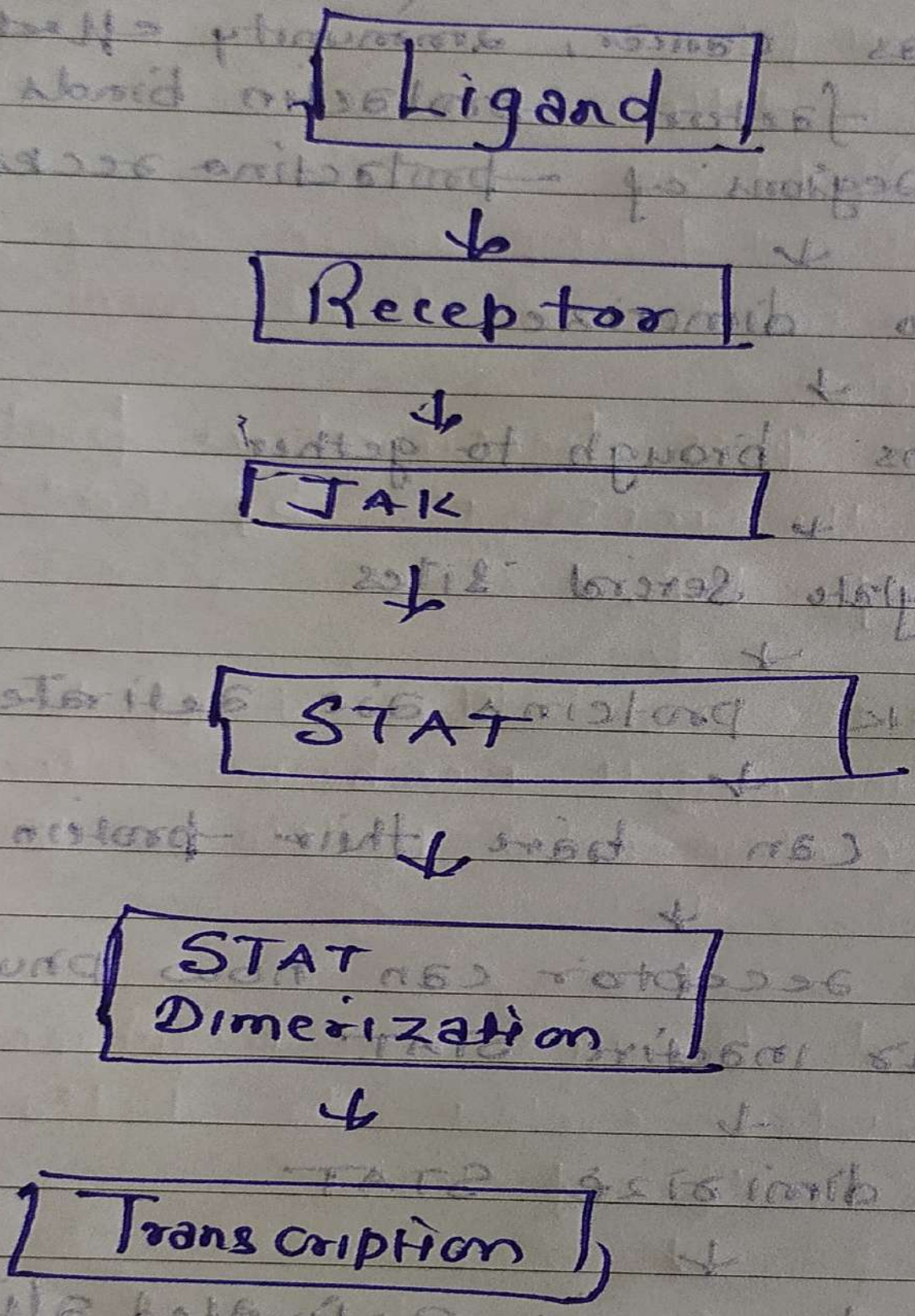
Activated STAT Translocate into nucleus.

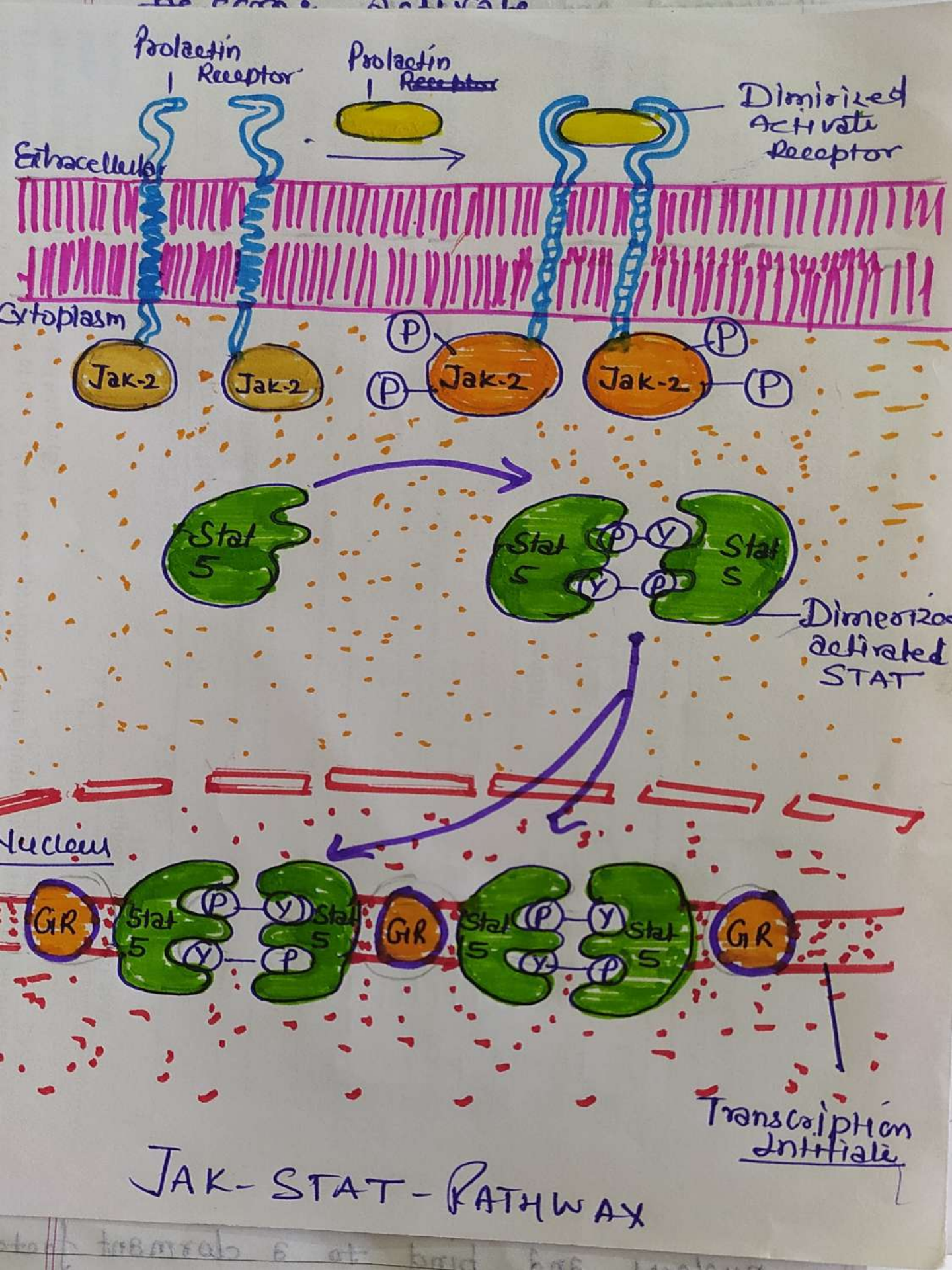
↓

Bind with specific regions of DNA

↓

Start transcription


Ligand
Receptor
JAK
STAT
STAT
Dimerization
Transcription


Prolactin Receptor
Prolactin Receptor
Dimerized Activated Receptor
Extracellular
Cytoplasm
Jak-2
Jak-2
Jak-2
Jak-2
P
Stat 5
Stat 5
Stat 5
Y
Dimerized activated STAT
Nucleus
GR
GR
GR
Transcription Initiate
JAK-STAT-PATHWAY