

Receptors: key structures in cell signaling

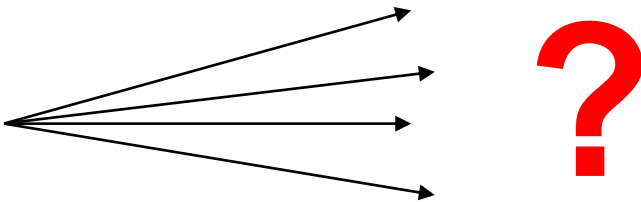
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Signal transduction in multicellular organism

- Humoral signaling
- Neuronal signaling

Signal transduction in multicellular organism

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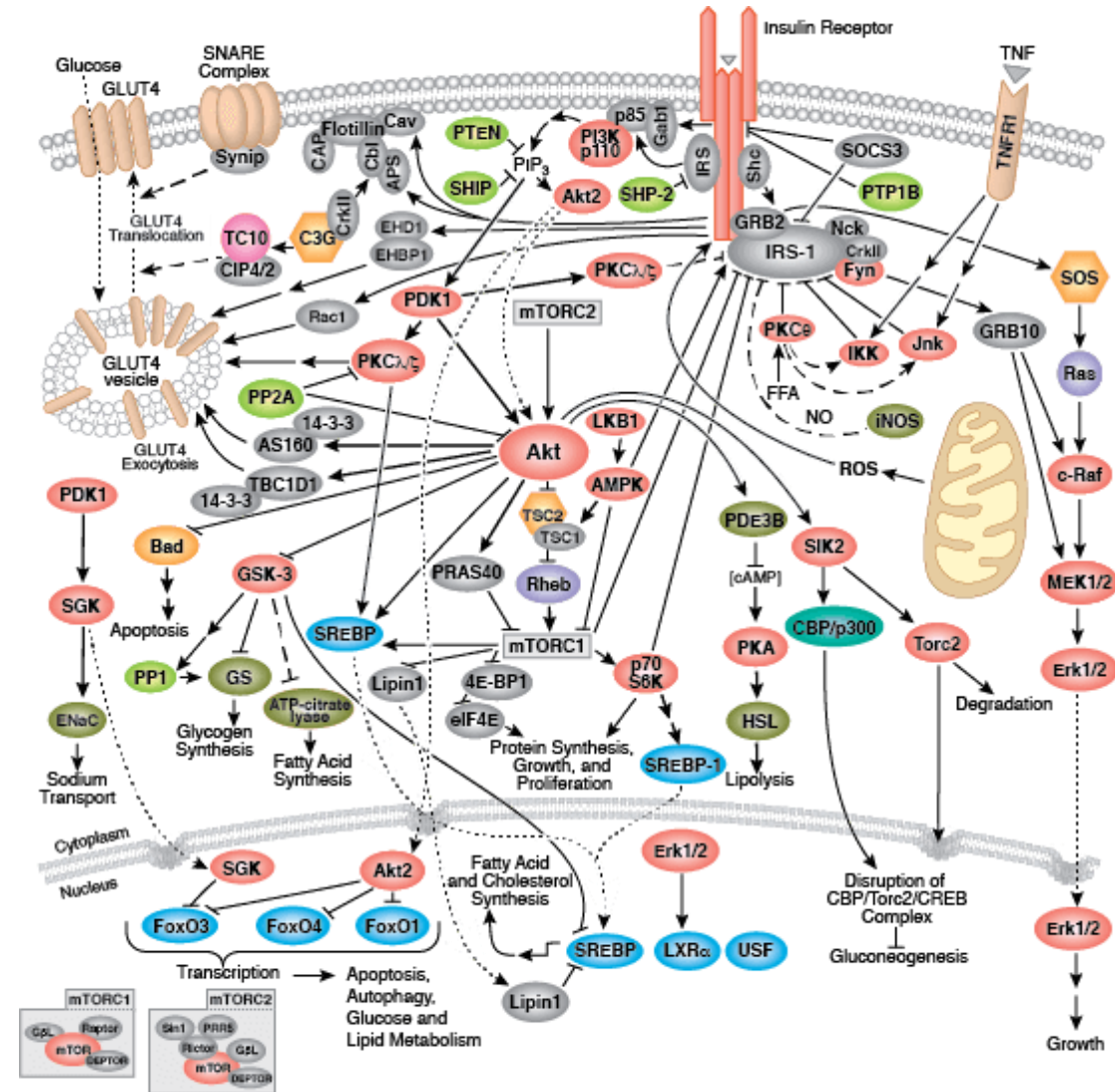
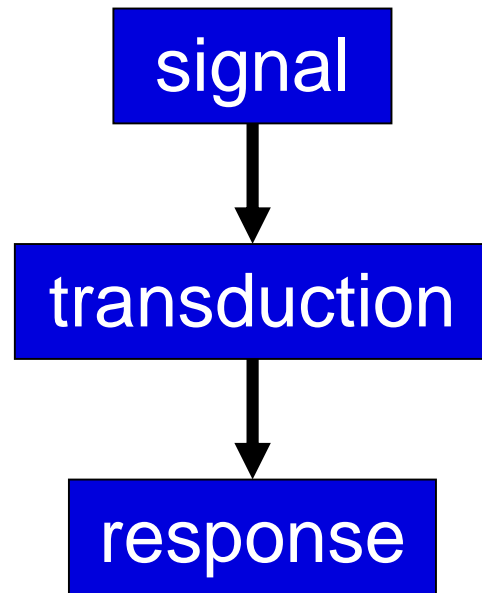
Signal transduction in multicellular organism

– Humoral signaling

– Neuronal signaling

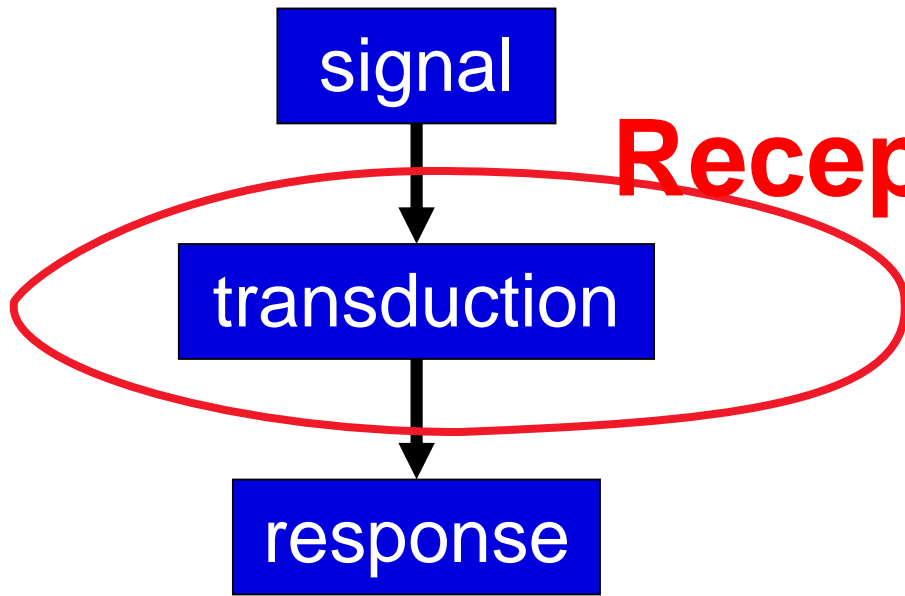


Cellular signaling

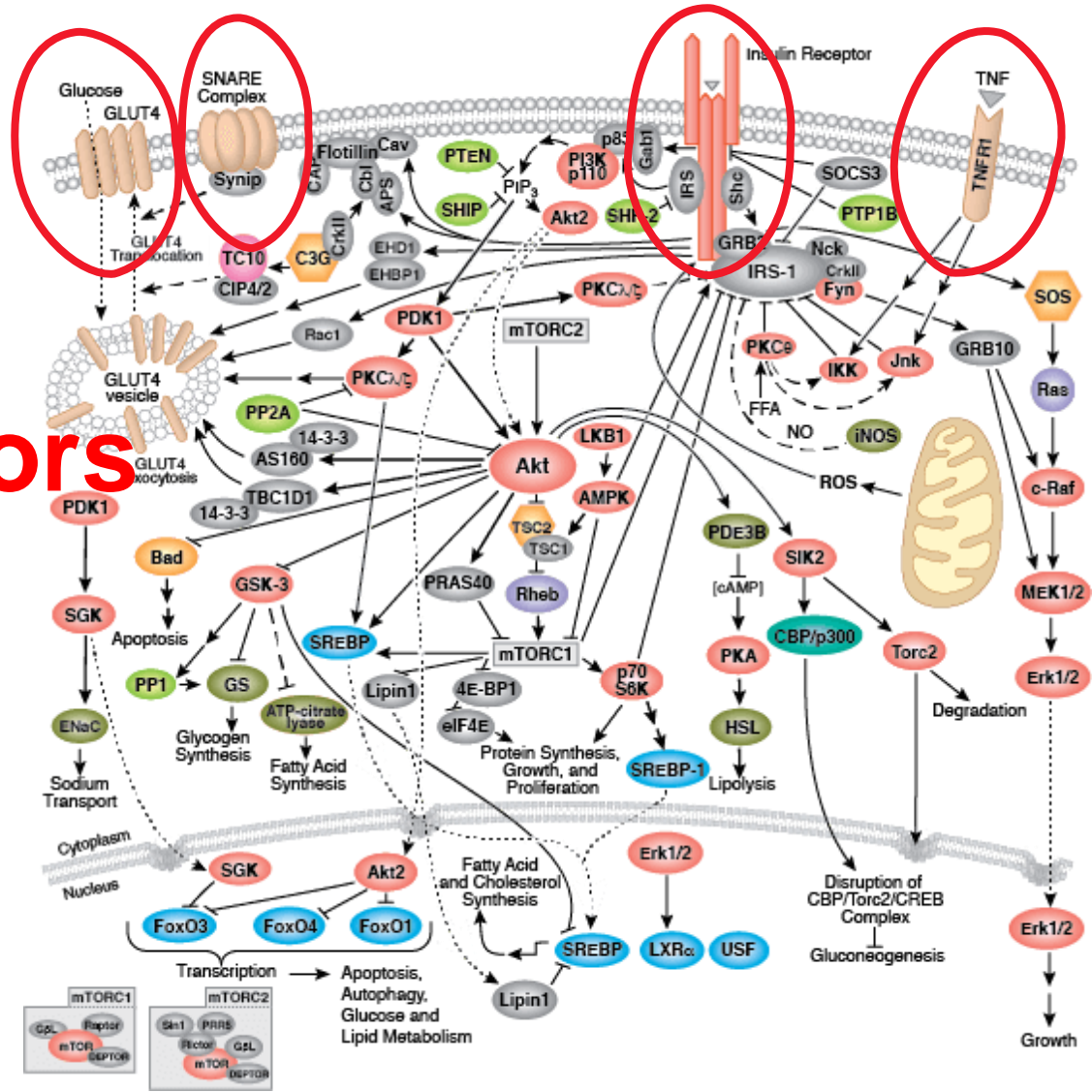


<https://www.cellsignal.com/contents/science-cst-pathways-cellular-metabolism/insulin-receptor-signaling/pathways-irs>

Cellular signaling



Receptors



<https://www.cellsignal.com/contents/science-cst-pathways-cellular-metabolism/insulin-receptor-signaling/pathways-irs>

Receptors

- Protein-based structures
- Receive and transduce signals
- Integrated in signaling pathways

Classification

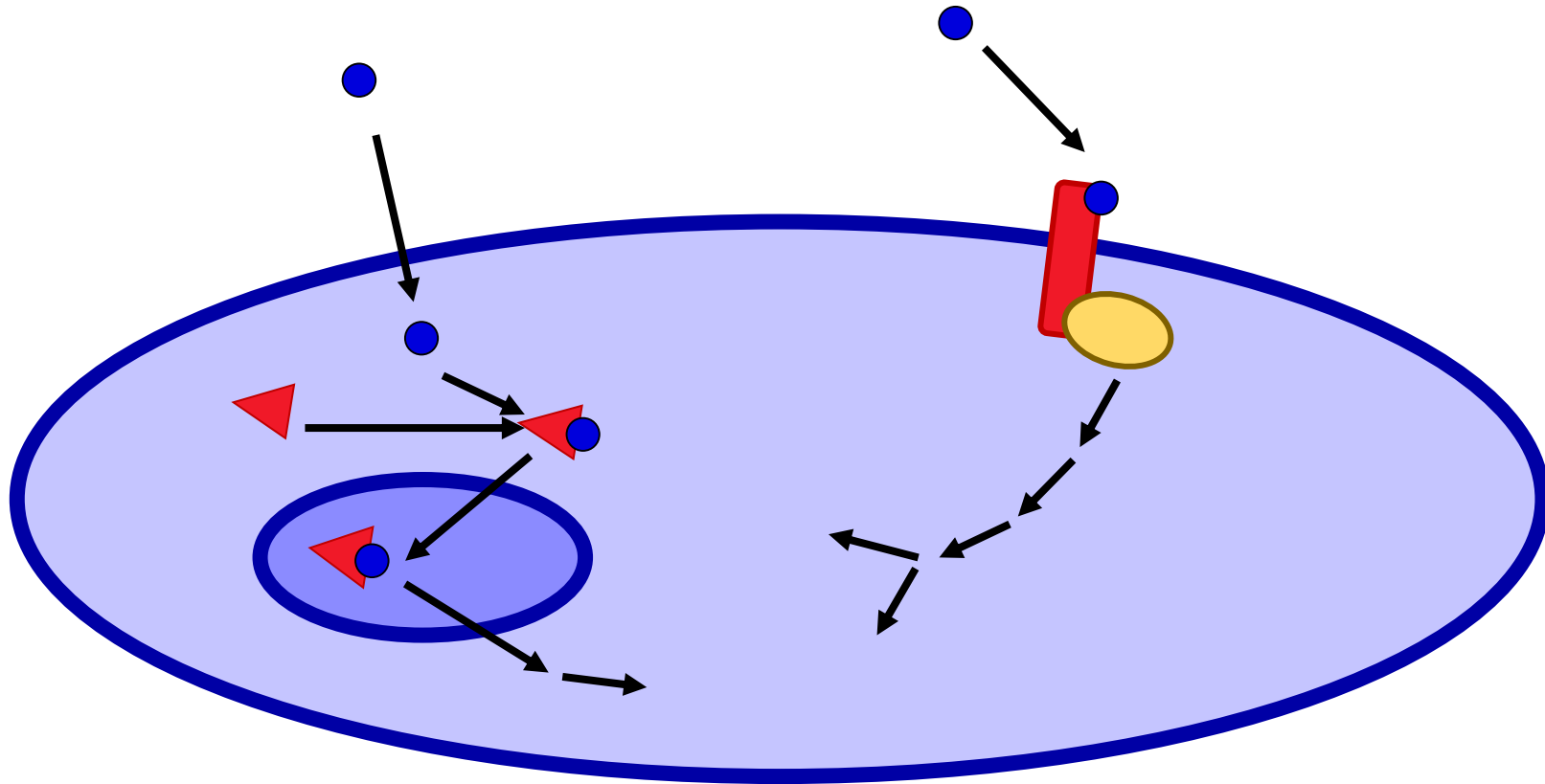
– Location:

- Intracellular
- Cell surface

– Function

- Ionotropic = ligand-gated ion channels
- G protein-coupled
- Enzyme-linked
 - Tyrosine kinases
 - Histidine kinases

Intracellular vs. cell-surface receptors



Ionotropic receptors

- Ligand-gated ion channels
- Direct change of membrane voltage and/or intracellular concentration of the ion

Metabotropic receptors

- Production of second messenger
- G protein-coupled receptors
- Enzyme-linked receptors
 - Receptor Tyrosine kinases
 - Receptor Histidine kinases

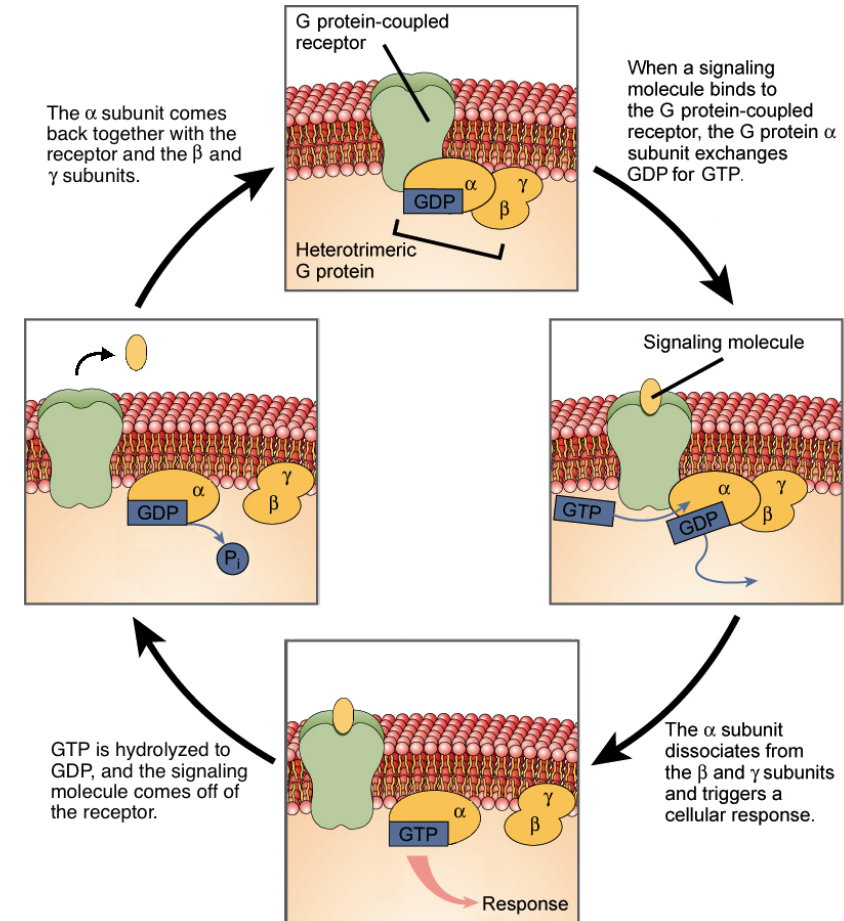
G protein-coupled receptors

– Production of second messenger:
cAMP, cGMP, DAG, IP3, Ca²⁺

– G_s

– G_i

– G_q

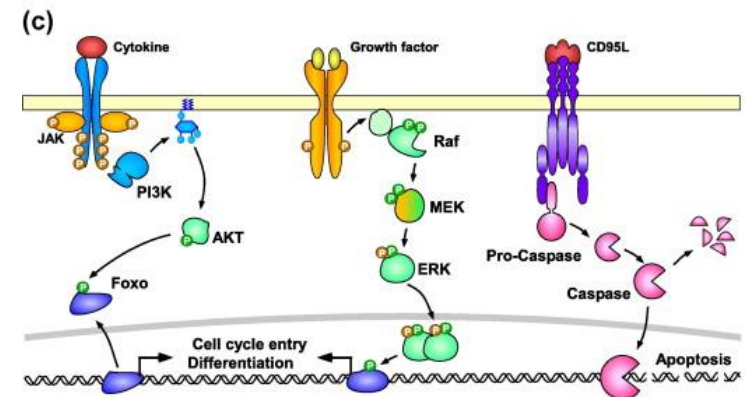
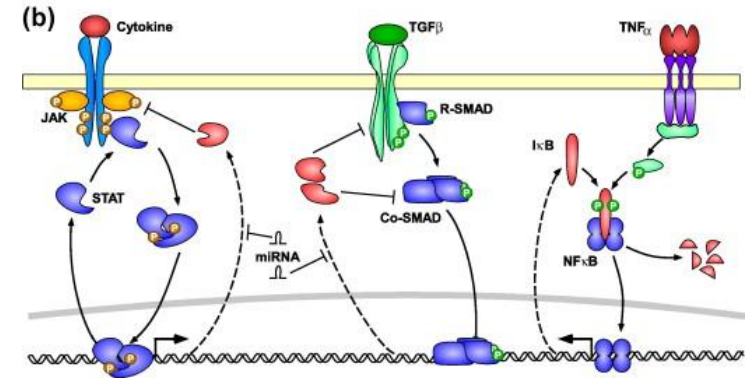
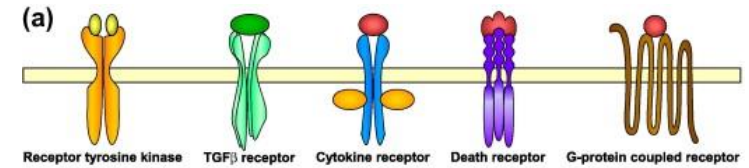


<https://www.khanacademy.org/science/biology/cell-signaling/mechanisms-of-cell-signaling/a/signal-perception>

Enzyme-linked receptors

Receptor tyrosine kinases

- Tyrosine kinase activity -
phosphorylation of enzymes/other
proteins



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Regulation of receptor response

Down-regulation

- Decrease of number and/or sensitivity of the receptors due to increased ligand stimulation
- Desensitisation
- Internalisation

Regulation of receptor response

Up-regulation

- Increase of number and/or sensitivity of the receptors due to decreased ligand stimulation
- (Re)sensitisation
- Externalisation
- Synthesis de novo

Receptor families

- Classification according to **ligand(s)**

Adrenergic receptors

- G protein-coupled receptors
- Subtypes:
 - Alpha:
 - $\alpha 1$ (Gq) – DAG+IP3; smooth muscle contraction, mydriasis
 - $\alpha 2$ (Gi) – cAMP; platelet activation
 - Beta (Gs) - cAMP
 - $\beta 1$ – heart (SA node)
 - $\beta 2$ – smooth muscle relaxation (bronchodilation)
 - $\beta 3$ – lipolysis, urination

Acetylcholine (cholinergic) receptors

- M type = Muscarinic acetylcholine receptors

- Metabotropic receptors – G-protein coupled receptors

- Subtypes

- M1 – CNS, autonomic ganglia, salivary glands, stomach

- M2 – heart (SA node, atria, AV node), CNS

- M3 – smooth muscle (e.g. vessels, bronchi), endocrine+exocrine glands, GIT, eyes, CNS

- M4+M5 – CNS

- N type = Nicotinic acetylcholine receptors

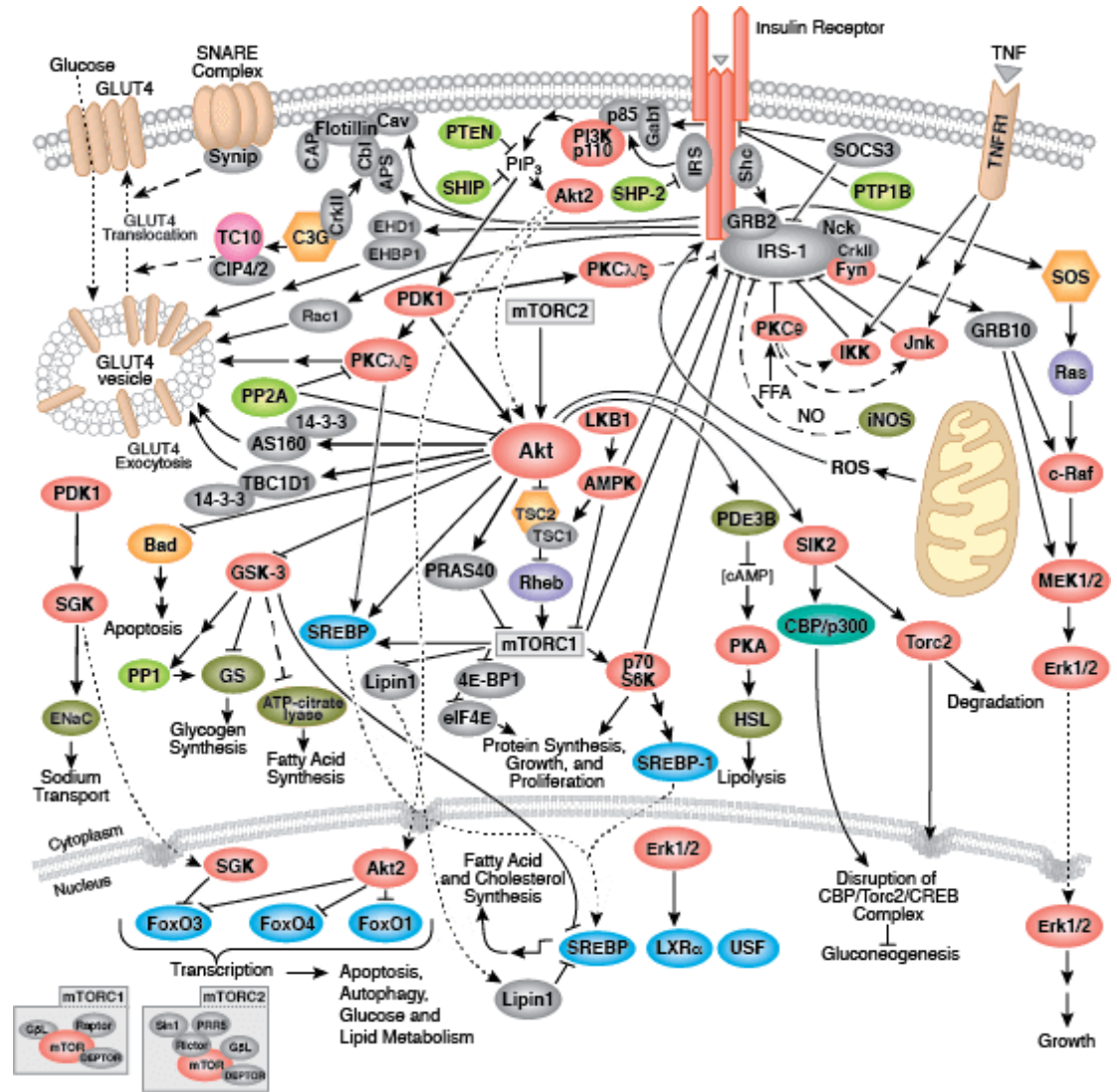
- Ionotropic receptors – ligand-gated ion channels

- Subtypes (according to subunits)

- Nm – „muscular“ type – neuromuscular junction

- Nn – „neuronal“ type – autonomic ganglia, adrenal medulla

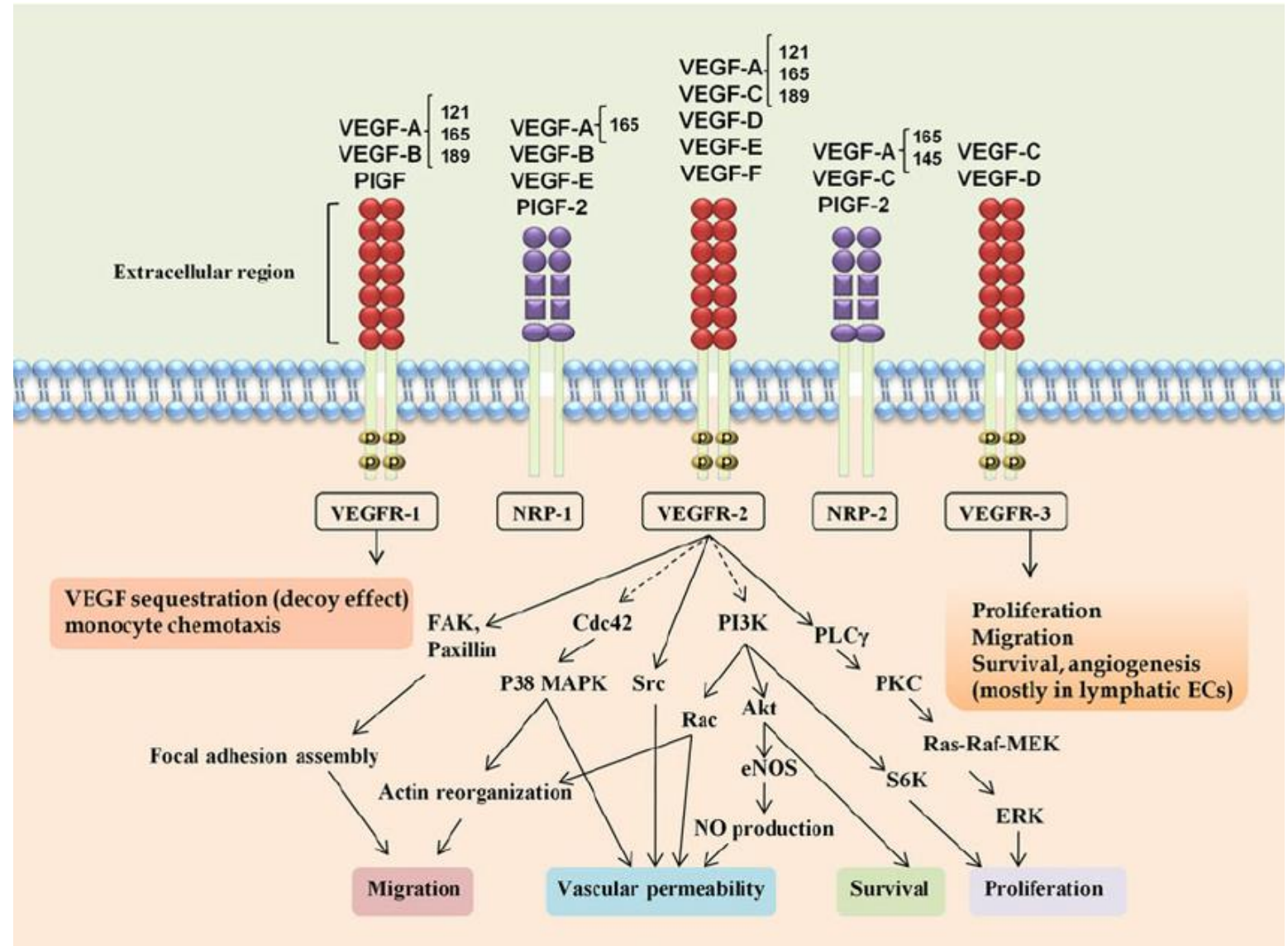
Insulin receptors



<https://www.cellsignal.com/contents/science-cst-pathways-cellular-metabolism/insulin-receptor-signaling/pathways-irs>

VEGFR

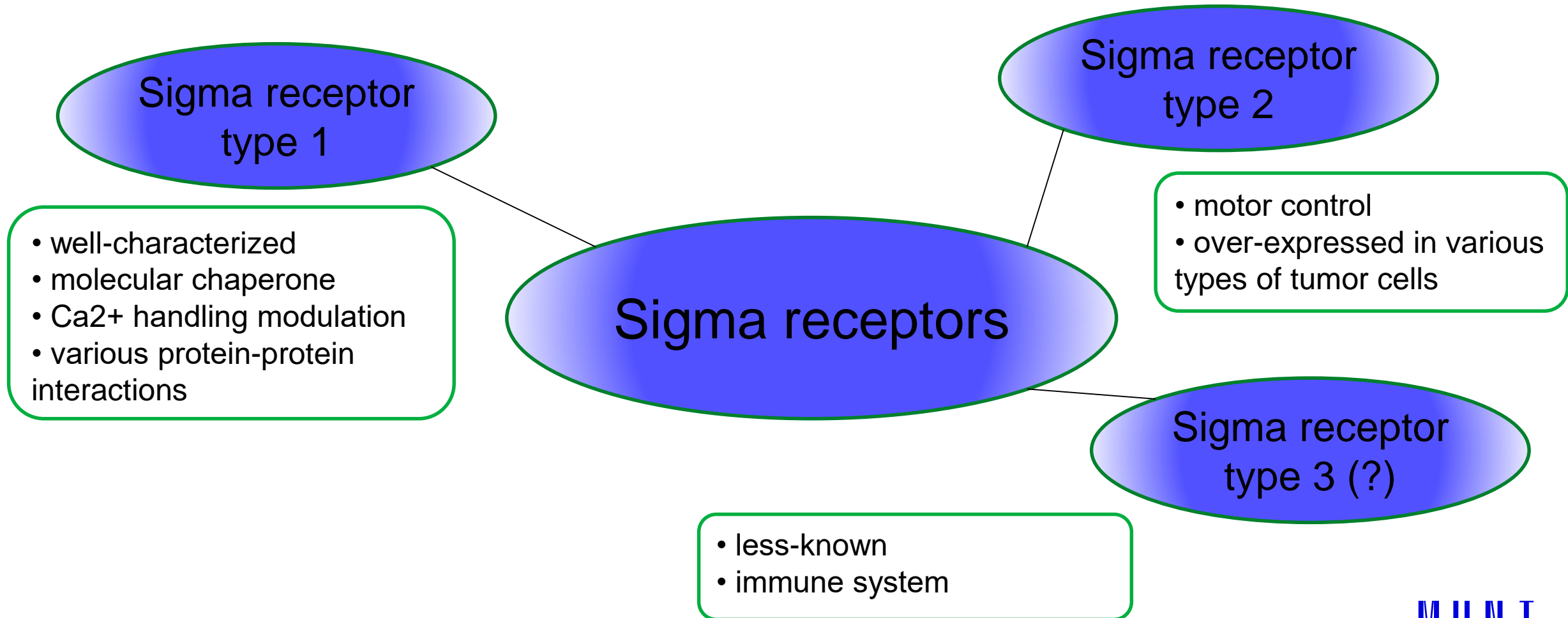
– Vascular
endothelial
growth factor
receptor



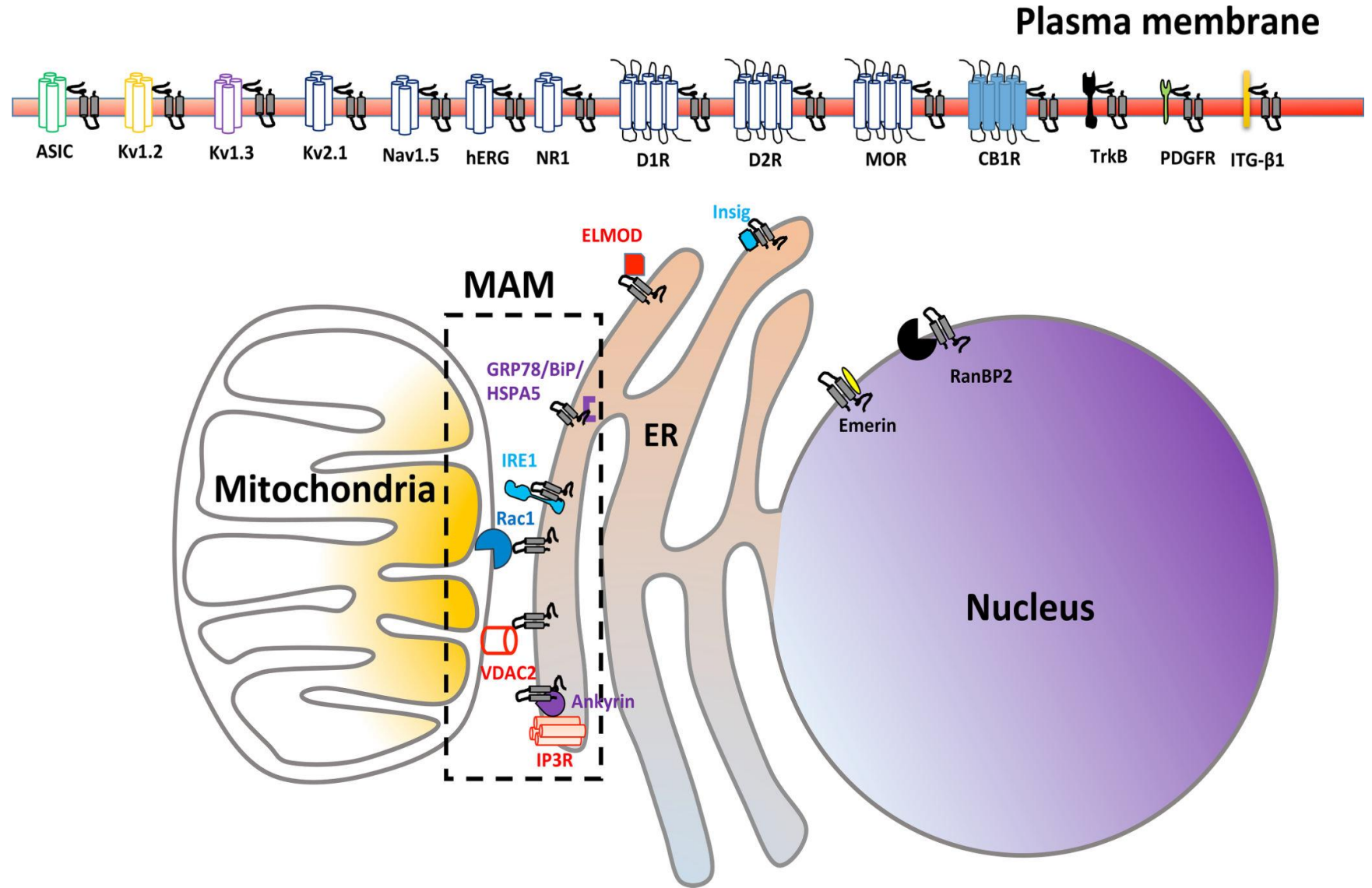
IP3 receptors

- Inositol-tris-phosphate receptors

Sigma receptors



Sigma 1 R



Su et al., 2016.
Trends Pharmacol Sci. 2016; 37(4): 262–278. doi:10.1016/j.tips.2016.01.003

Take home message

Receptors are

- crucial structures in cell signalling.
- important in pathophysiology of many diseases.
- targets of pharmacotherapy.

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