

Receptory: klíčové struktury v buněčné signalizaci

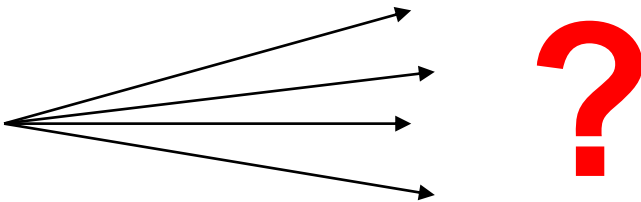
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Audiovizuální obsah prezentovaný během on-line přednášky je autorským dílem vytvořeným zaměstnanci Masarykovy univerzity. Jakékoliv další šíření tohoto obsahu nebo jeho části bez svolení Masarykovy univerzity je v rozporu se zákonem.

Signal transduction in multicellular organism

- Humoral signaling
- Neuronal signaling

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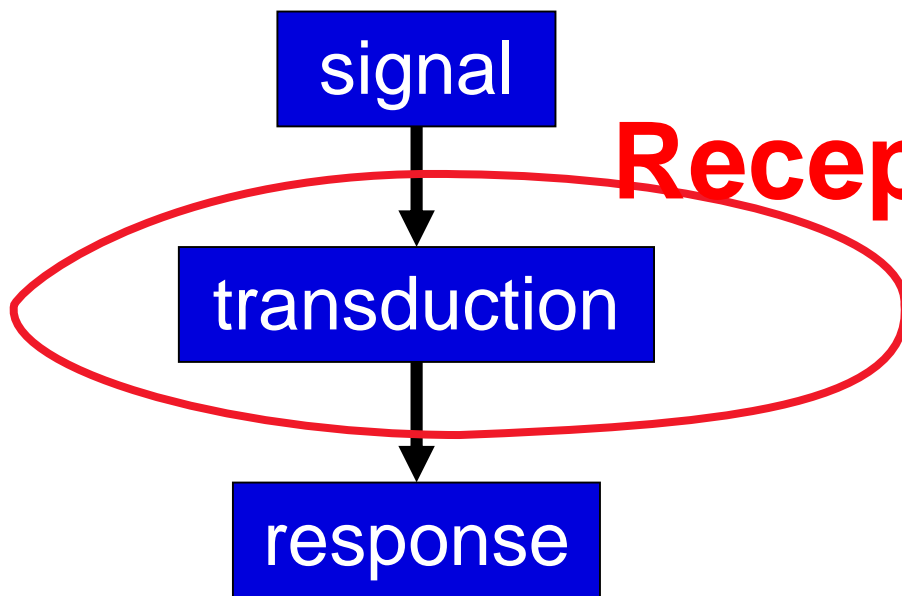
Signal transduction in multicellular organism

– Humoral signaling

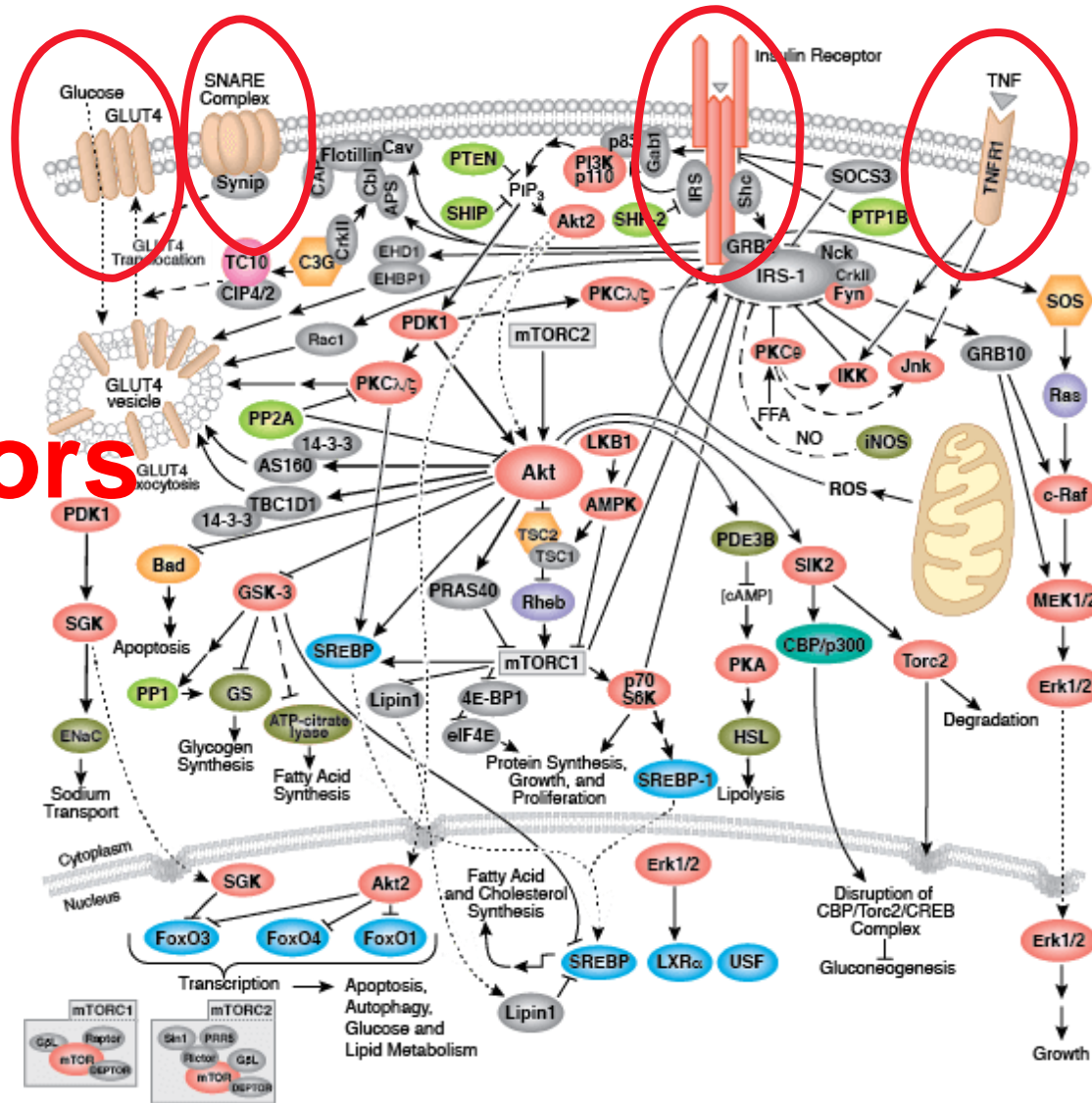
– Neuronal signaling



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

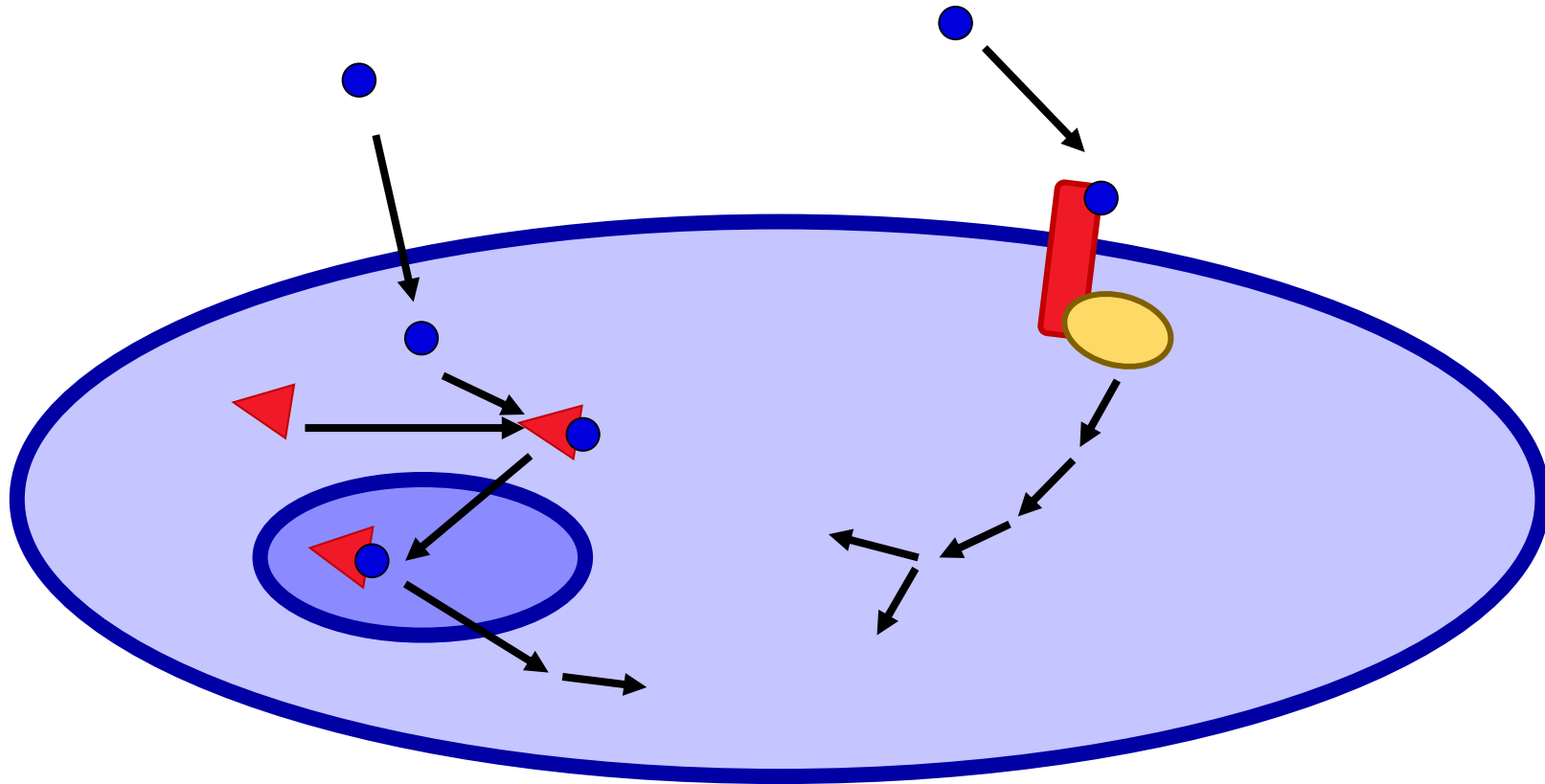
– Location:

- 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

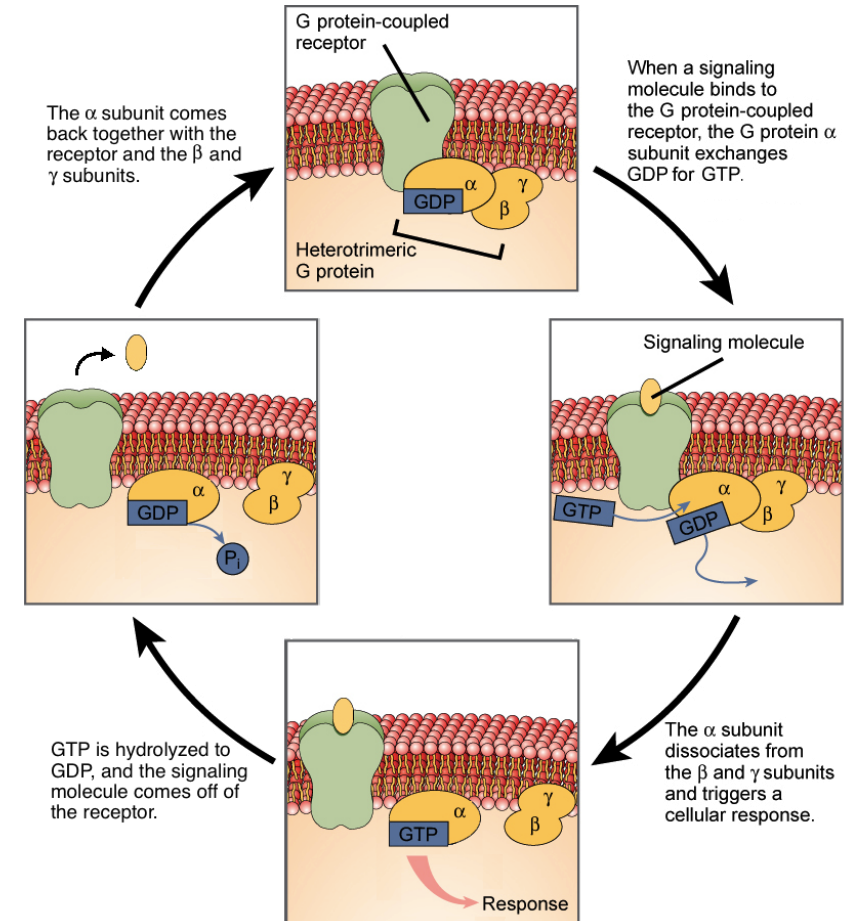
G protein-coupled receptors

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

– G_s

– G_i

– G_q

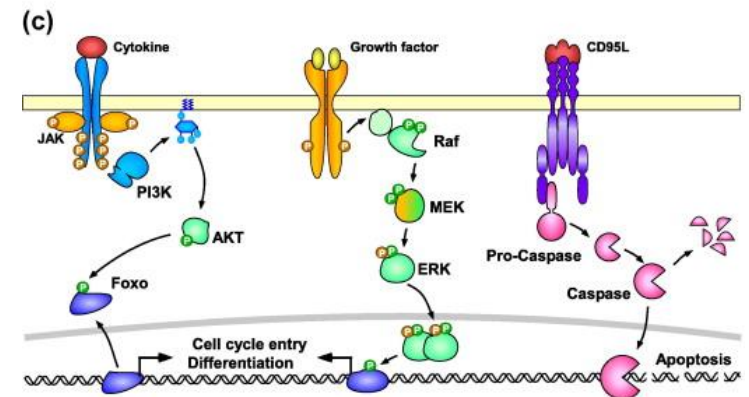
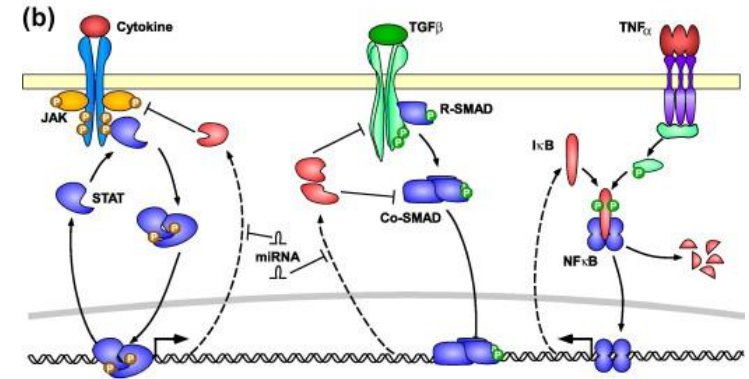
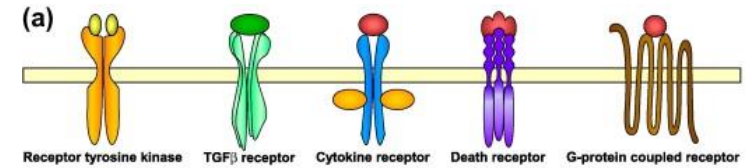


<https://www.khanacademy.org/science/biology/cell-signaling/mechanisms-of-cell-signaling/a/signal-perception>

Enzyme-linked receptors

Receptor tyrosine kinases

- Tyrosine kinase activity -
phosphorylation of enzymes/other
proteins



https://ars.els-cdn.com/content/image/3-s2.0-B978012405926900046-f04-04-9780124059269.jpg?_

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

- Ligands: catecholamines
 - Epinephrine (adrenaline)
 - Norepinephrine (noradrenaline)
 - Dopamine

Adrenergic receptors - subtypes

– Alpha:

- $\alpha 1$ (Gq) – DAG+IP3; smooth muscle contraction, mydriasis
- $\alpha 2$ (Gi) – cAMP; platelet activation

– Beta (Gs)

- $\beta 1$ – heart (SA node)
- $\beta 2$ – smooth muscle relaxation (bronchodilation)
- $\beta 3$ – lipolysis, urination

Dopamine receptors

- G protein-coupled receptors
- Ligand: dopamine
- Expression:
 - CNS – neurotransmission, neuromodulation
 - peripheral (non-)neural tissues

Dopamine receptors - subtypes

- D1-like family (Gs): D1, D5
- D2-like family (Gi): D2, D3, D4

- Dimerization
 - Heterodimers (e.g. D1-D2)
 - Non-isoreceptor heterodimers (e.g. D2-Adenosine A2R)
- Protein interactions

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

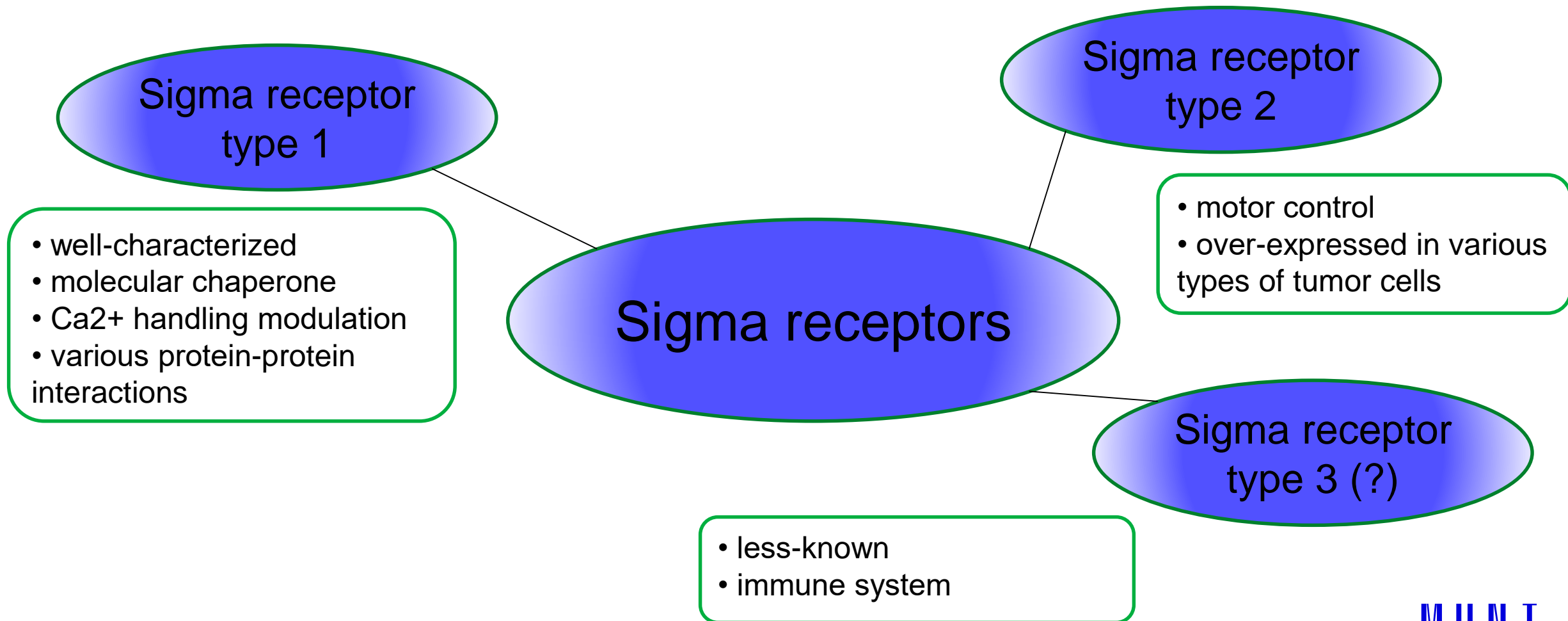
Vascular endothelial growth factor (VEGF) receptors

- Membrane (mbVEGFR) or soluble (sVEGFR) receptors
- Three main subtypes: VEGFR-1, VEGFR-2, VEGFR-3
- Tyrosine kinase activity
- Vasculogenesis, angiogenesis

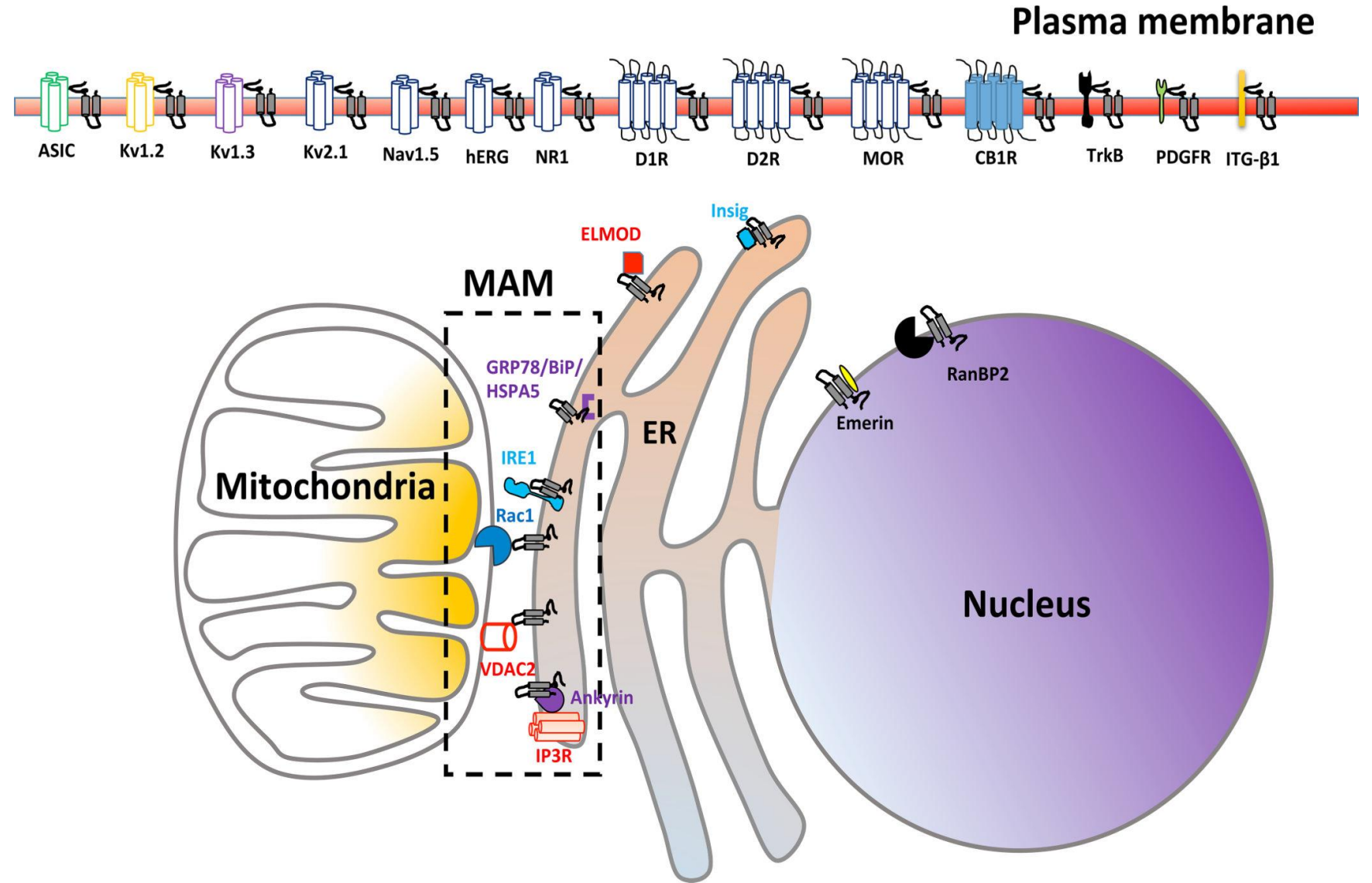
Inositol-tris-phosphate (IP3) receptors

- Intracellular receptors - endoplasmic reticulum, mitochondria
- Types: IP3R1, IP3R2, IP3R3
- Function: ligand-gated Ca²⁺ channels
- Dimerisation and proteinprotein interactions

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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