

# **Receptors: key structures in cell signaling**

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# Signal transduction in multicellular organism

- Neuronal signaling
- Humoral signaling





# Receptors

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

# Classification

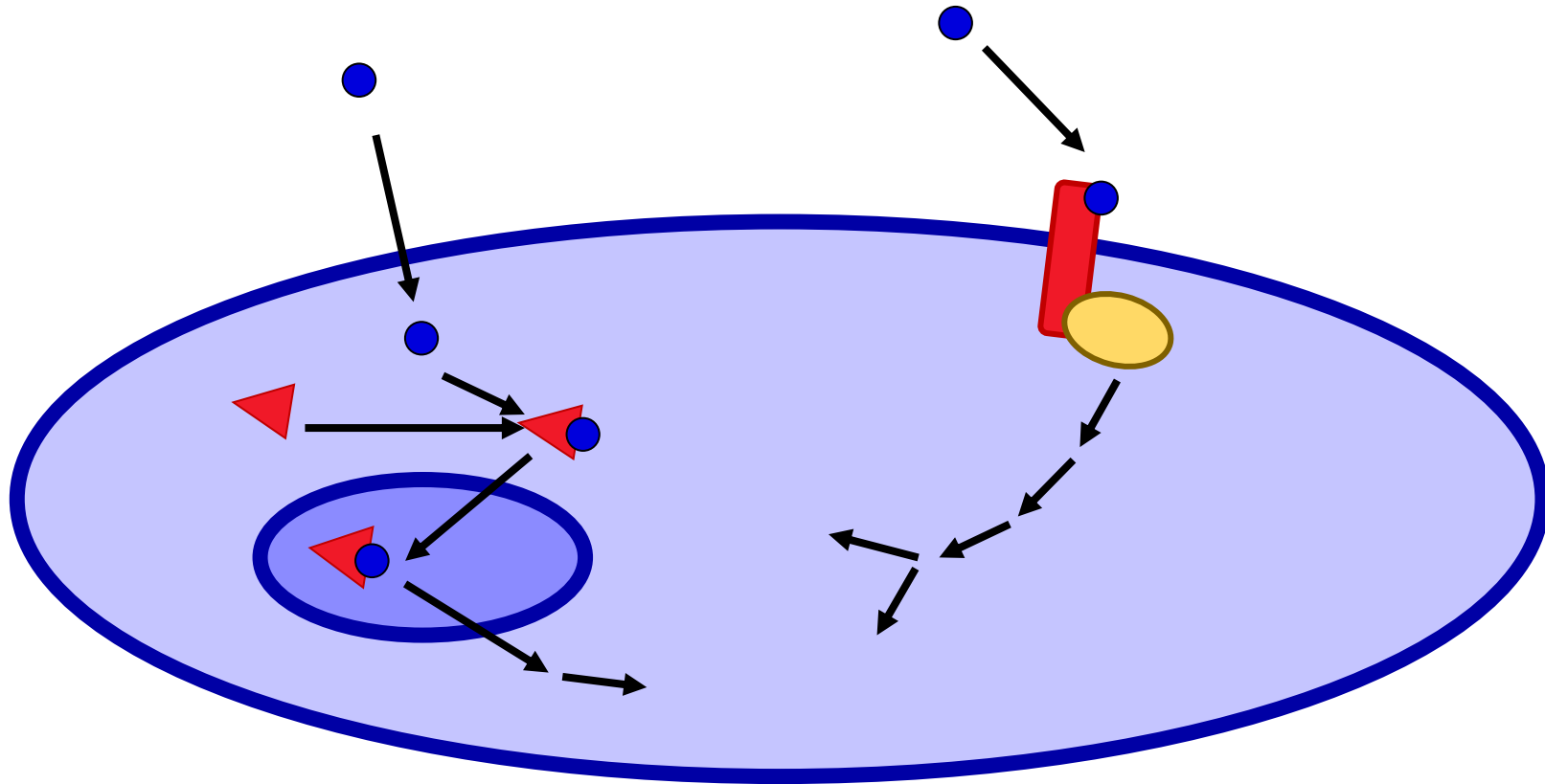
## – Location:

- 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

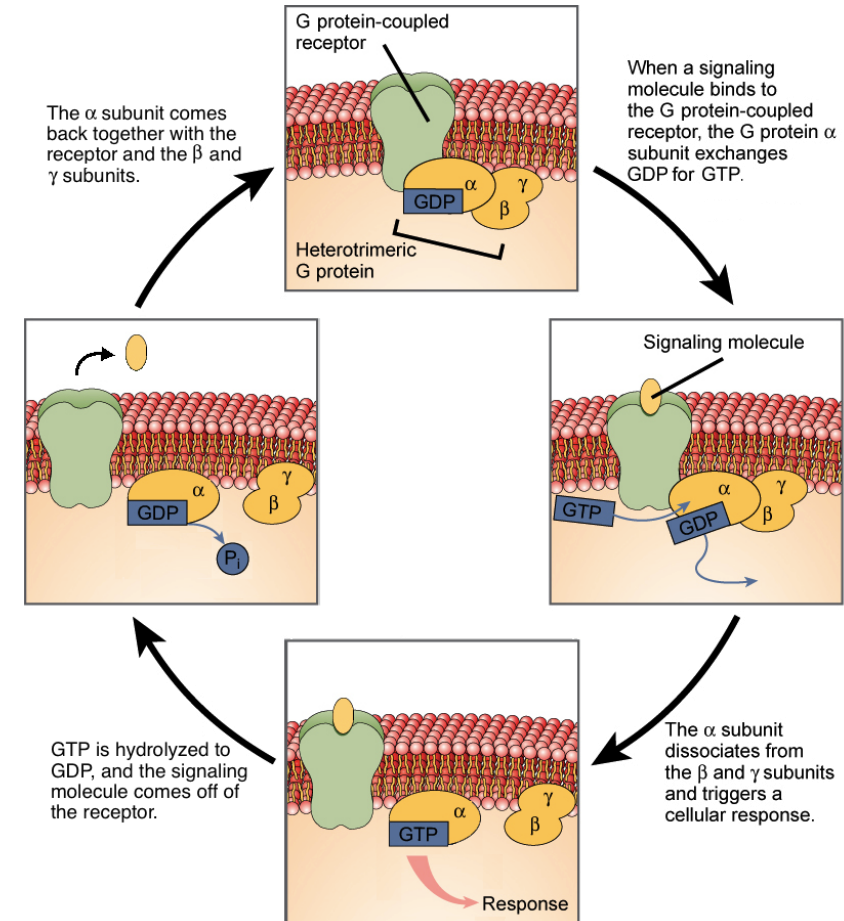
# G protein-coupled receptors

– Production of second messenger:  
cAMP, cGMP, DAG, IP3, Ca<sup>2+</sup>

– G<sub>s</sub>

– G<sub>i</sub>

– G<sub>q</sub>

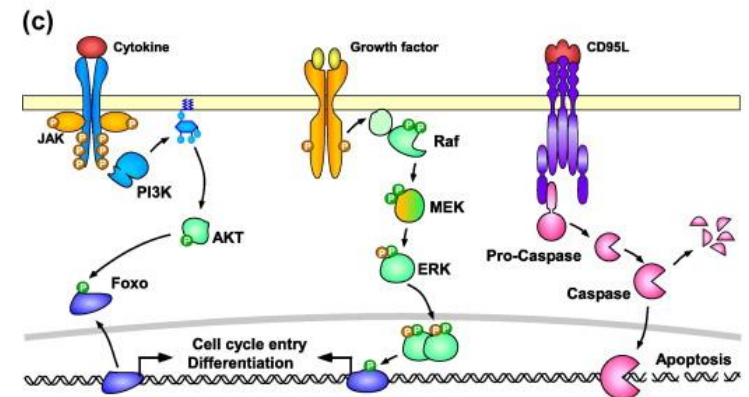
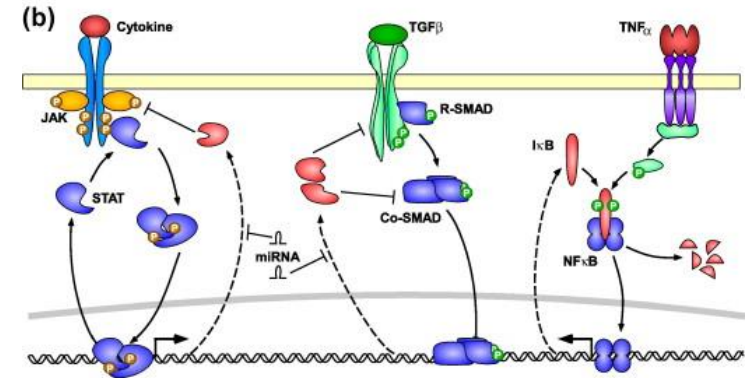
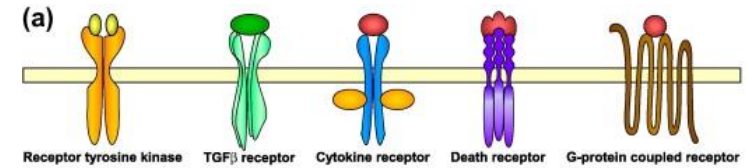


<https://www.khanacademy.org/science/biology/cell-signaling/mechanisms-of-cell-signaling/a/signal-perception>

# 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

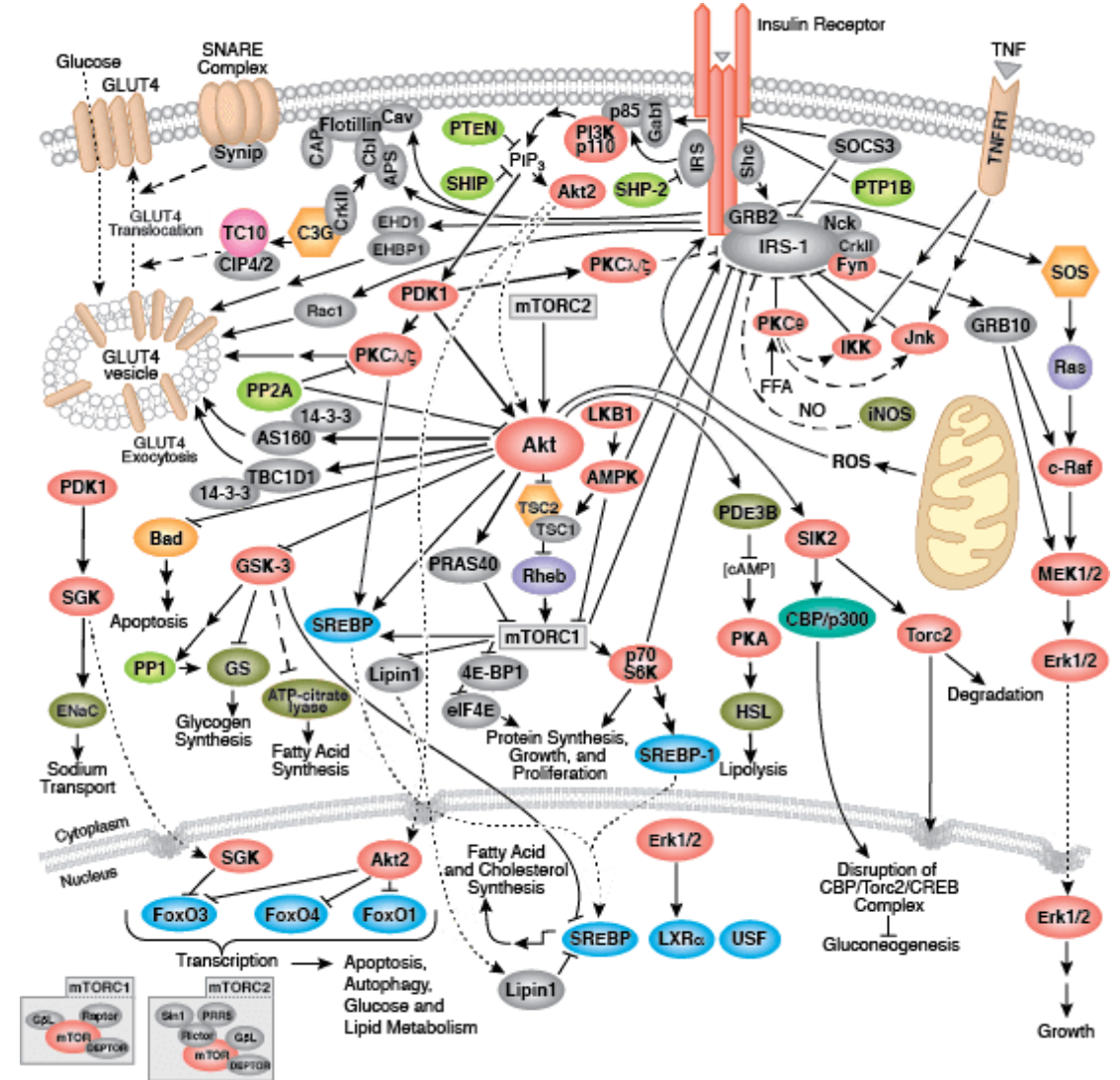


# Insulin receptor

– ligands: insulin, IGF-I, IGF-II

– 2 subunits

– tyrosine kinase activity



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

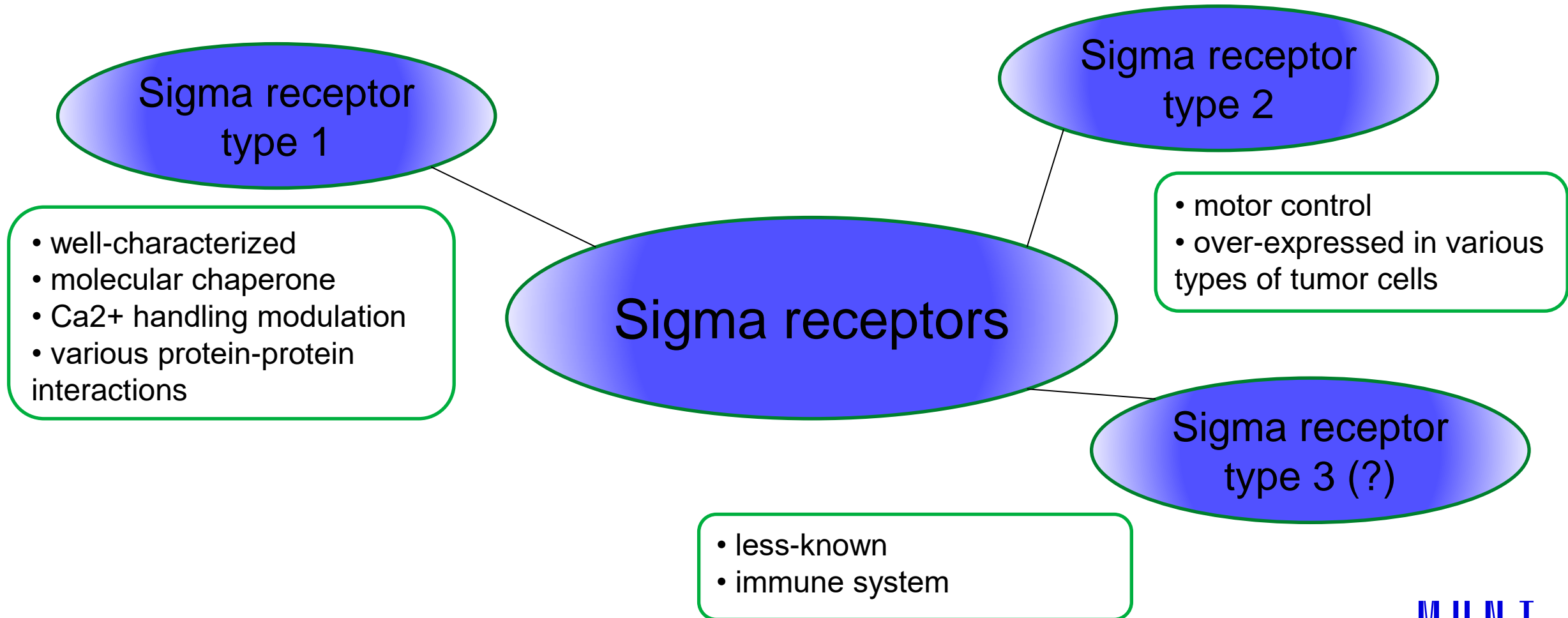
# Vascular endothelial growth factor (VEGF) receptors

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

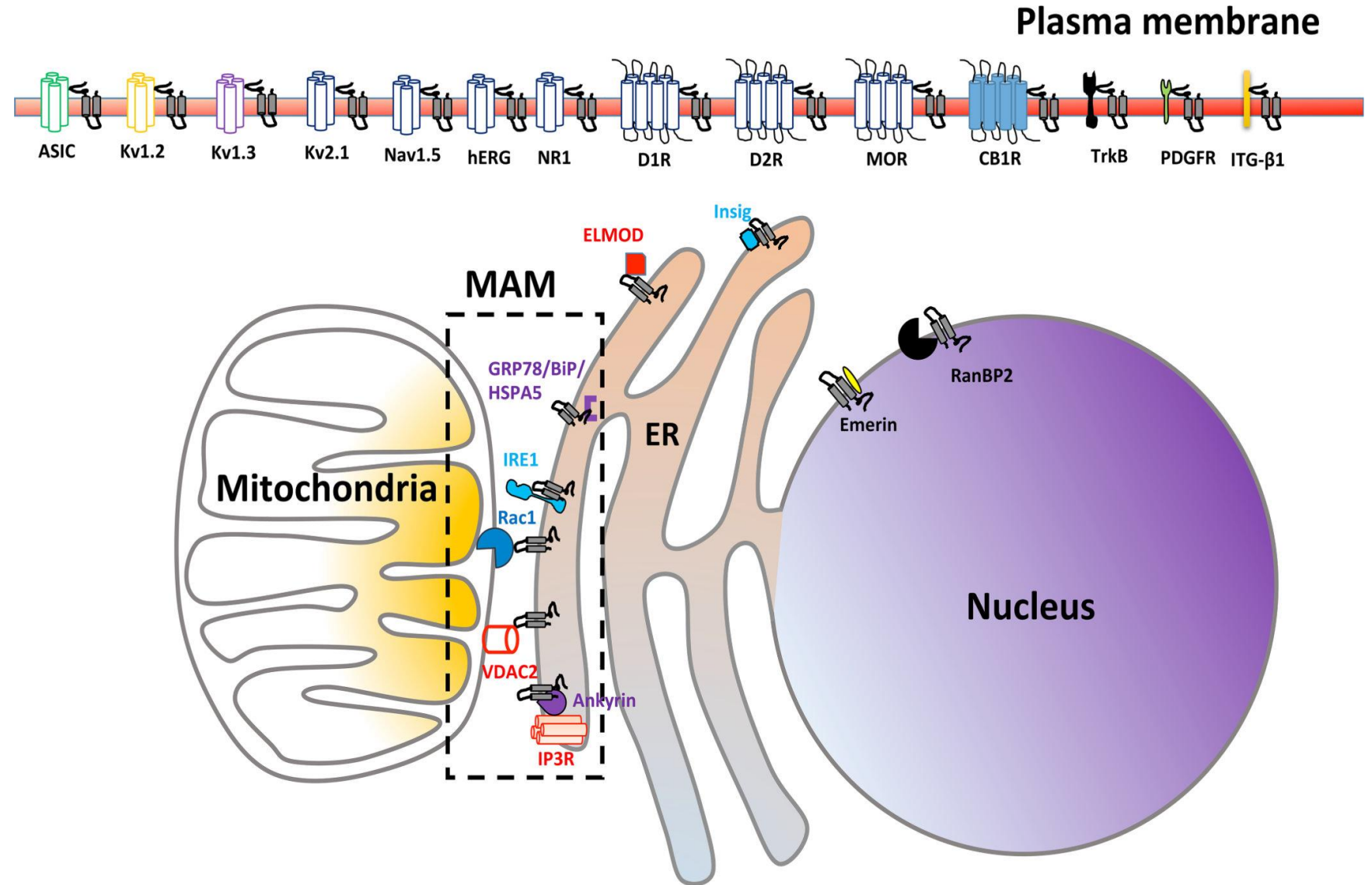
# Inositol-tris-phosphate (IP3) receptors

- Intracellular receptors - endoplasmic reticulum, mitochondria
- Types: IP3R1, IP3R2, IP3R3
- Function: ligand-gated Ca<sup>2+</sup> 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 signaling
- important in pathophysiology of many diseases
- targets of pharmacotherapy

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