Fats, Cholesterol, and Hormones

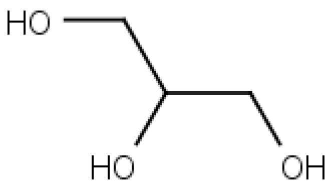
Types of Fats

Lipids – biological origin – sparingly soluble in water

Main classes of lipids

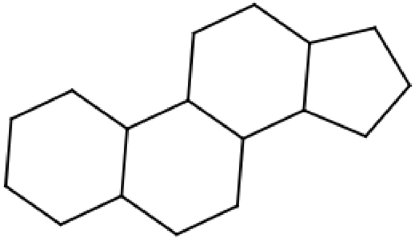
Fatty Acids – long hydrocarbon chains with a carboxylic acid on one end

Triacylglycerols – fatty acid derivatives of glycerol



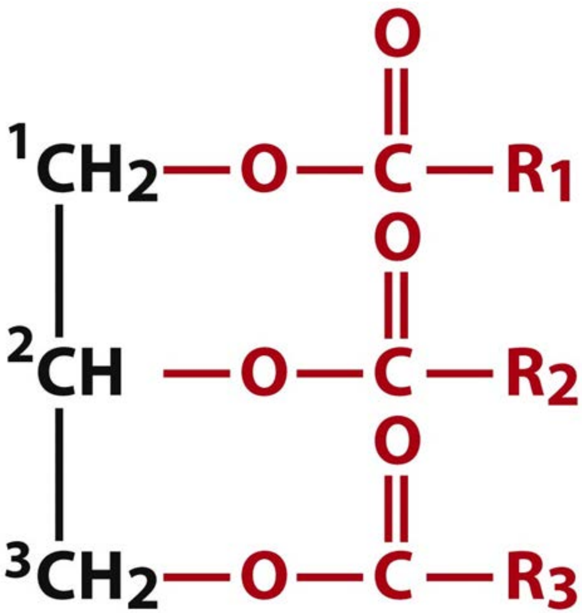
Phosphoacylglycerol–phosphate substituted diacylglycerols

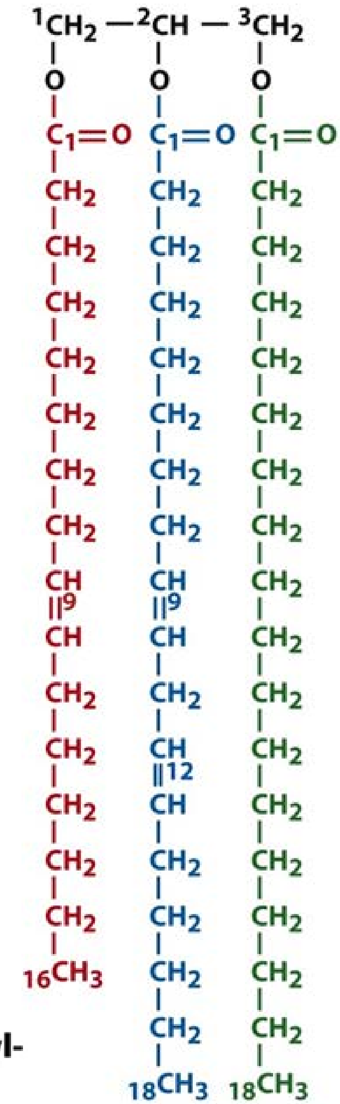
Cholesterol – 4 ring system with a single polar group



Triacylglycerol (ide)

Triacylglycerols – fatty acid derivatives of glycerol





1-Palmitoleoyl-2-linoleoyl-3-stearoyl-glycerol

Fatty Acids

Saturated – single bonds all the way down the chain

Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.6
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2

C > 20 or C < 14 are very uncommon

Most chains have an even number

Fatty Acids

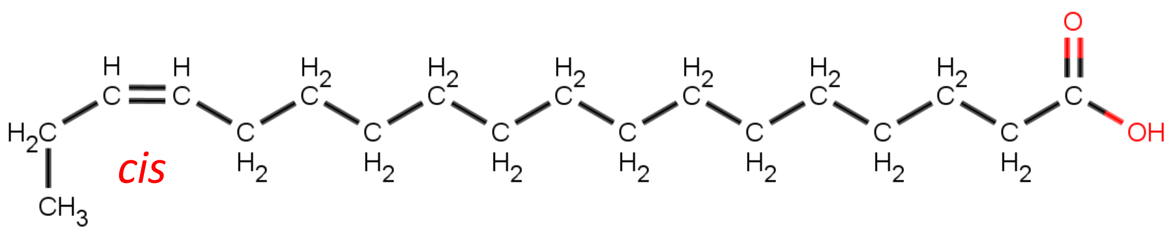
Unsaturated – single bonds all the way down the chain

16:1*n*–7	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1*n*–9	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.4
18:2*n*–6	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3*n*–3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3*n*–6	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4*n*–4	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5*n*–3	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
22:6*n*–3	DHA	4,7,10,13,16,19-Docosahexenoic acid	$CH_3CH_2(CH{=}CHCH)_6CH_2COOH$	
24:1*n*–9	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

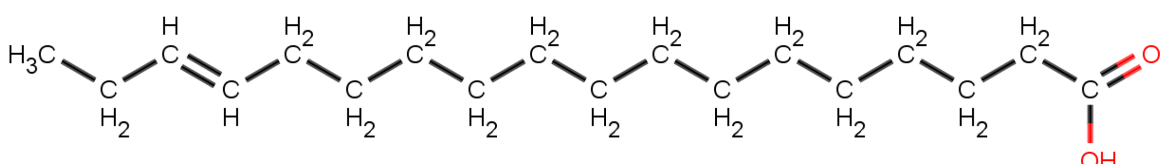
Chain length : number of double bonds - position of 1st double bond from CH_3 terminal

All double bonds are *cis*

Double bonds tend to form every 3 carbons



cis



trans

The importance of omega-3 FA

•**Blood fat (triglycerides).** Fish oil supplements can lower elevated triglyceride levels. Having high levels of this blood fat puts you at risk for heart disease. DHA alone has also been shown to lower triglycerides.

•**Rheumatoid arthritis.** Fish oil supplements (EPA+DHA) can curb stiffness and joint pain. Omega-3 supplements also seem to boost the effectiveness of anti-inflammatory drugs.

•**Depression.** Some researchers have found that cultures that eat foods with high levels of omega-3s have lower levels of depression. Fish oil also seems to boost the effects of antidepressants and may help the depressive symptoms of bipolar disorder.

•**Baby development.** DHA appears to be important for visual and neurological development in infants.

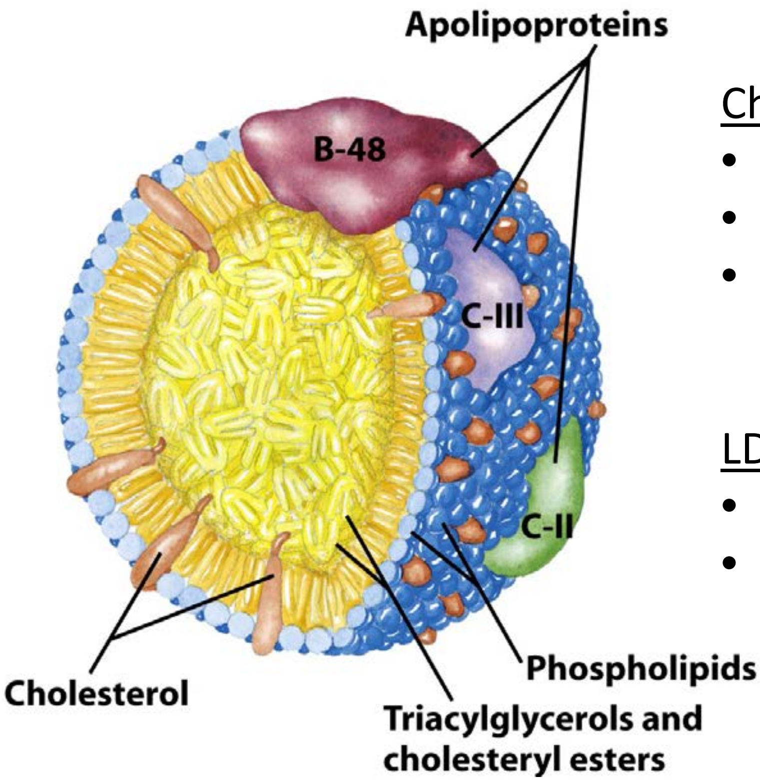
•**Asthma.** A diet high in omega-3s lowers inflammation, a key component in asthma. But more studies are needed to show if fish oil supplements improve lung function or cut the amount of medication a person needs to control the condition.

•**ADHD.** Some studies show that fish oil can reduce the symptoms of ADHD in some children and improve their mental skills, like thinking, remembering, and learning. But more research is needed in this area, and omega-3 supplements should not be used as a primary treatment.

•**Alzheimer's disease and dementia.** Some research suggests that omega-3s may help protect against Alzheimer's disease and dementia, and have a positive effect on gradual memory loss linked to aging. But that's not certain yet.

Source: WebMD

The Good, the Bad and the Ugly



Chlyomicrons

- Dietary fat/cholesterol transport to cells
- Originate in intestinal mucosa cells
- 1-2% protein, 85-88% triglycerides, ~8% phospholipids, ~3% cholesteryl esters and ~1% cholesterol

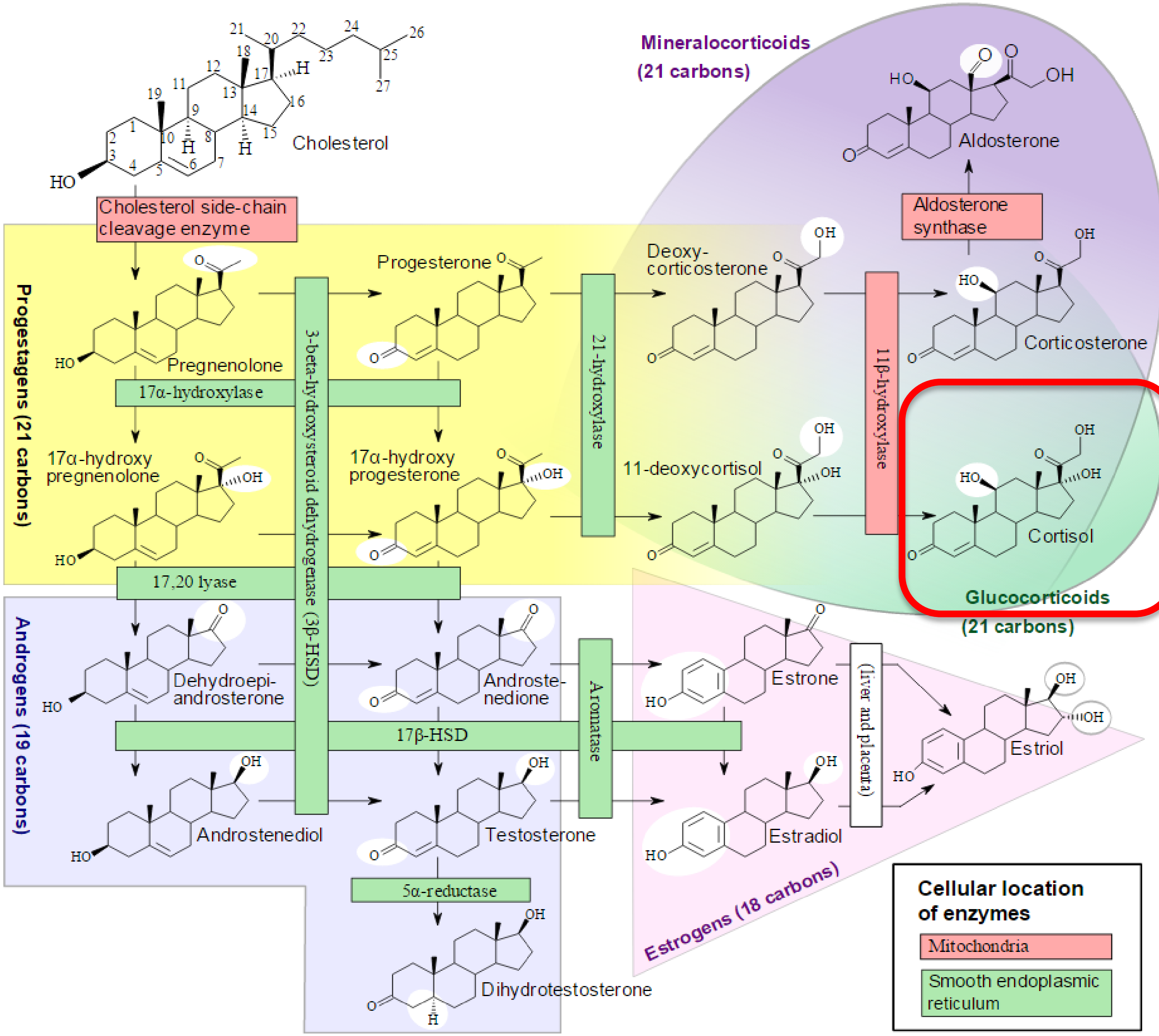
LDL (Low Density Lipoprotein) – "Bad" Cholestrol

- Cholesterol transport from liver to cells
- One of the lipoproteins (B-100) is recognized by LDL receptors. This triggers encapsulation of LDL and release of cholesterol to be used in the plasma membrane
- 20-22% protein, 10-15% triglycerides, 20-28% phospholipids, 37-48% cholesteryl esters, and 8-10% cholesterol

HDL (High Density Lipoprotein)

- Cholesterol transport to liver for degradation (or recycling)
- Cholesterol "scavenger"
- 55% protein, 3-15% triglycerides, 26-46% phospholipids, 15-30% cholesteryl esters, and 2-10% cholesterol

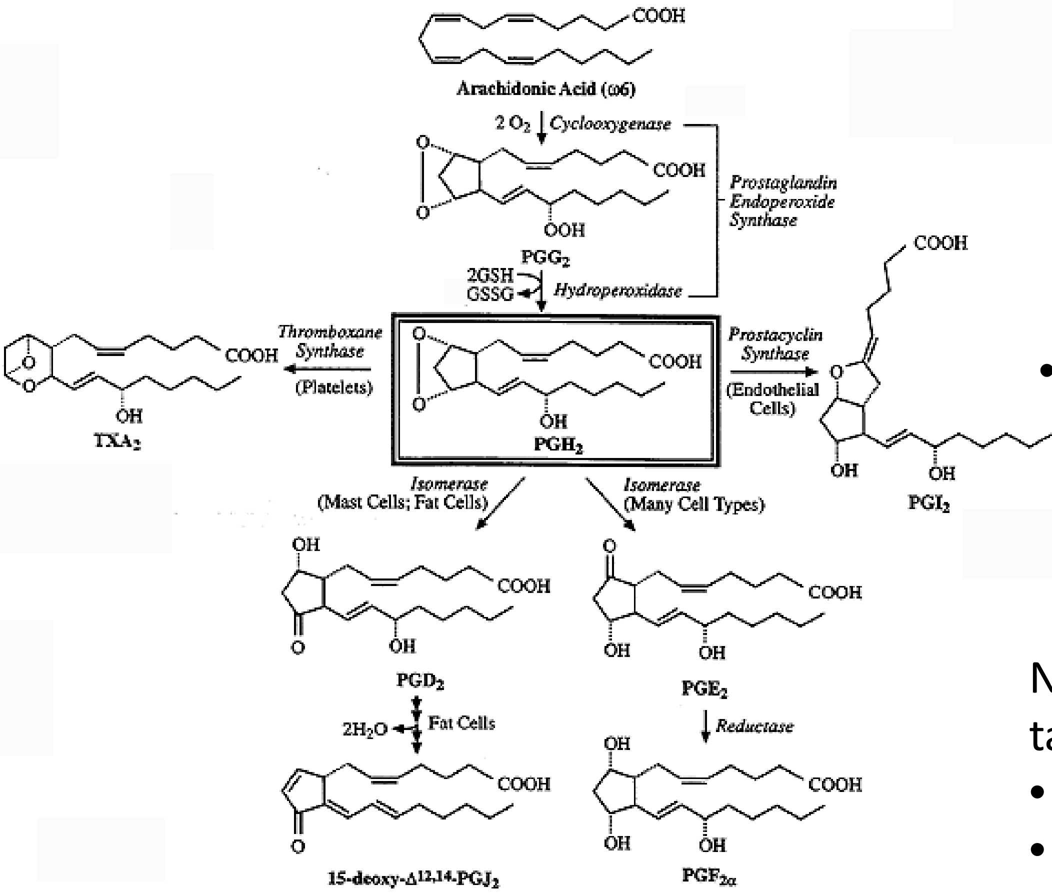
Steroid Hormones



Related to stress and low blood glucose response

Omega 6's and Prostaglandin Hormones

Synthesized in your body from Linoleic Acid



Some of the physiological effects of Prostaglandins:

- The inflammatory response (rheumatoid arthritis).
- The production of pain and fever.
- The regulation of blood pressure.
- The induction of blood clotting.
- The control of several reproductive functions such as the induction of labor.
- The regulation of the sleep / wake cycle.

Notable: Cyclooxygenase (COX-2) is the target of many anti-inflammatory drugs

- Aspirin
- Naproxen (Aleve)
- Ibuprofen (Motrin, Advil)

Hormones and Classifications

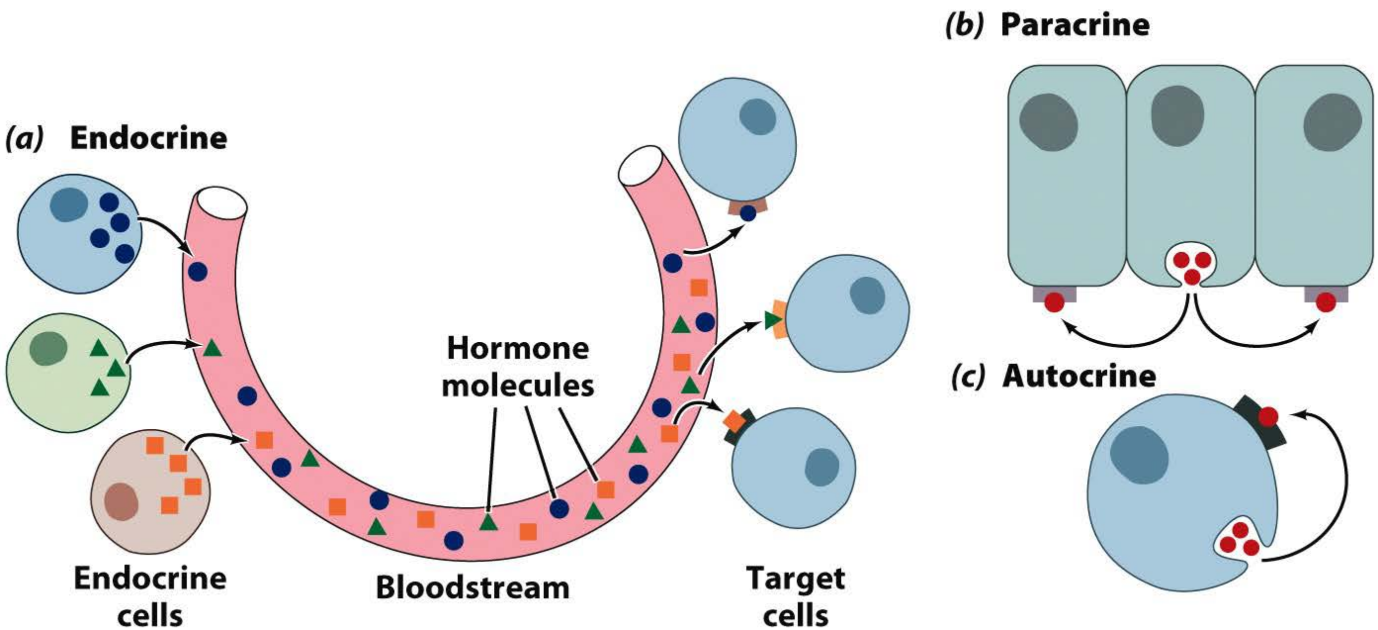
In eukaryotes, intercellular signals occur through mediated release of ***hormones*** (chemical messengers)

Classified by the distance over which the carry a message

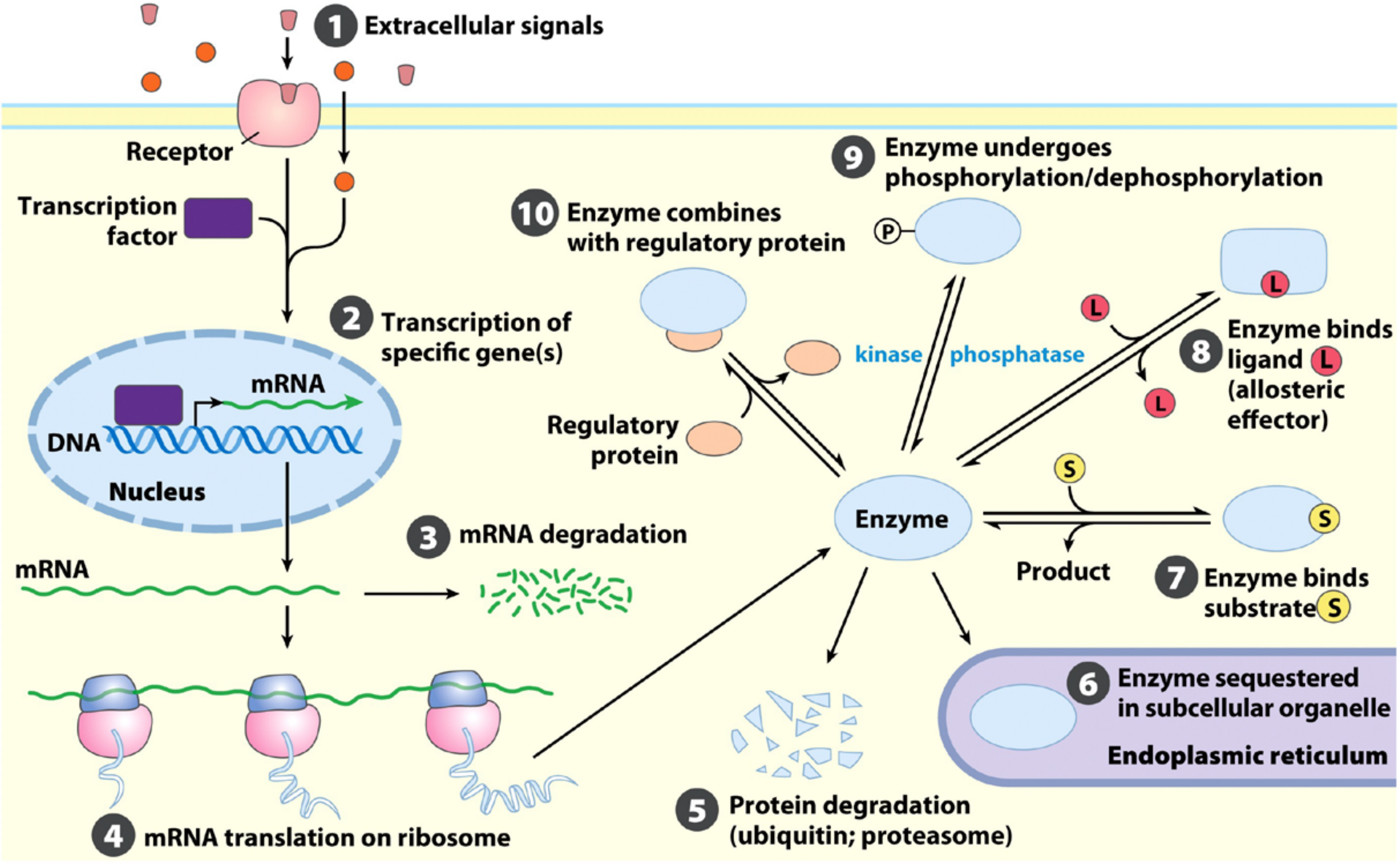
Endocrine hormones – act on cells distant from the site of release

Paracrine hormones – act on cells close to the site of release

Autocrine hormones – act on the same cell

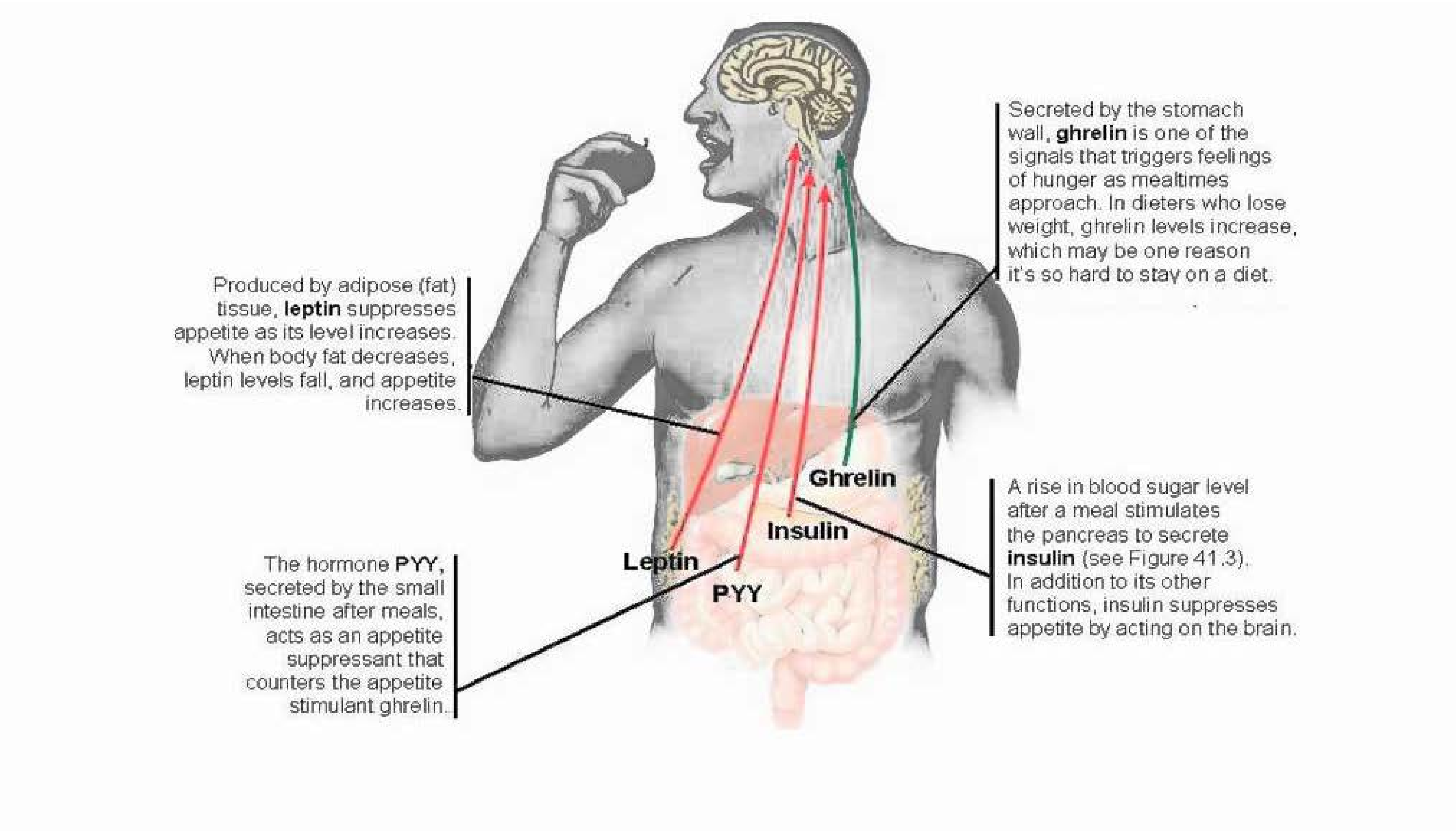


How do Hormones Work?



Hunger/Satiation

Hunger/Satiation



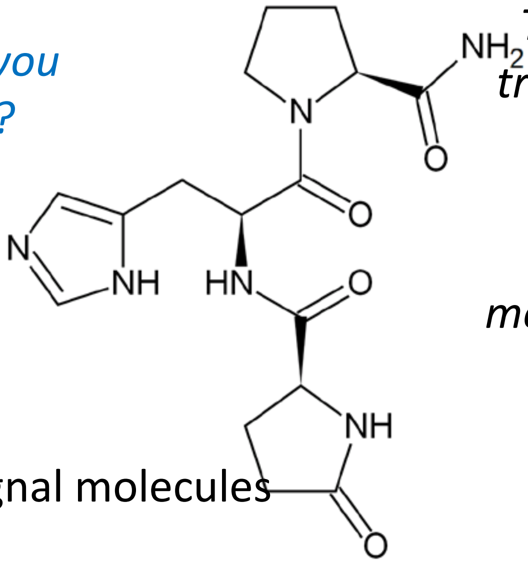
General Features of Signal Transduction

Specificity is achieved by precise molecular complementarity between the signal and receptor molecules

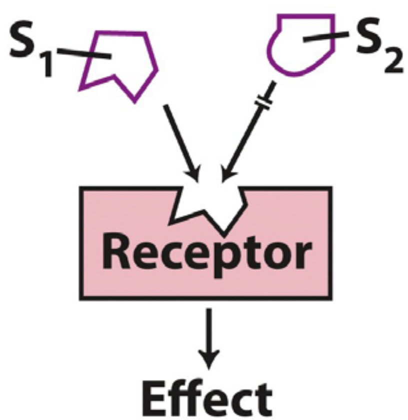
What types of IM forces do you think guide the specificity?

Extra specificity built into expression profile of certain cell types

Thyrotropin-releasing hormone triggers response in pituitary cells but not hepatocytes

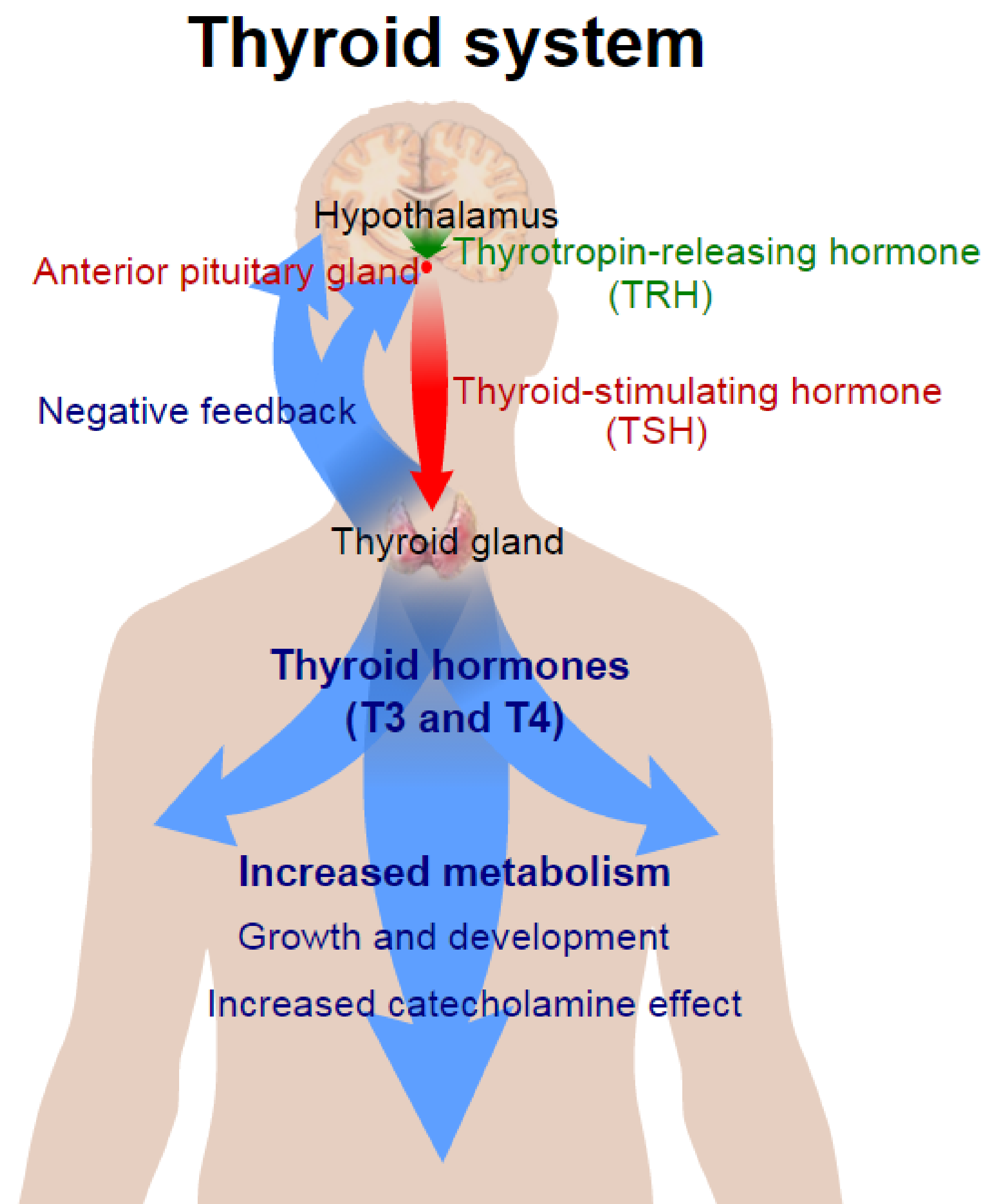


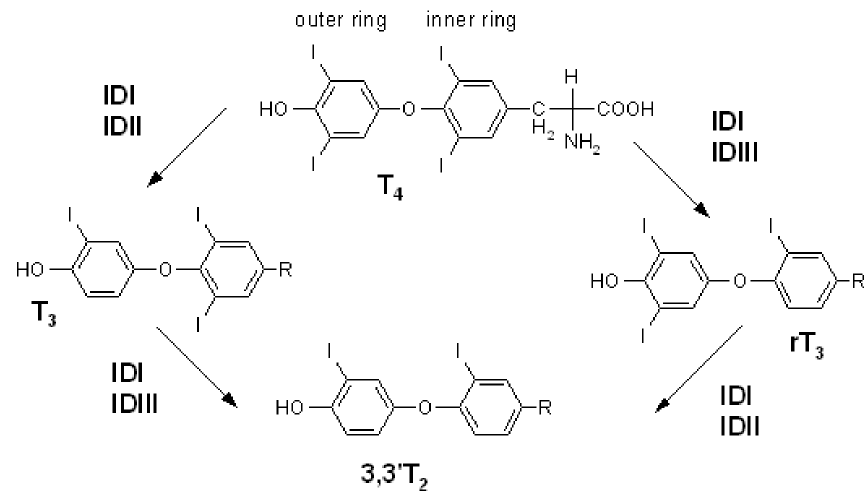
Epinephrine alters glycogen metabolism in hepatocytes but not adipocytes



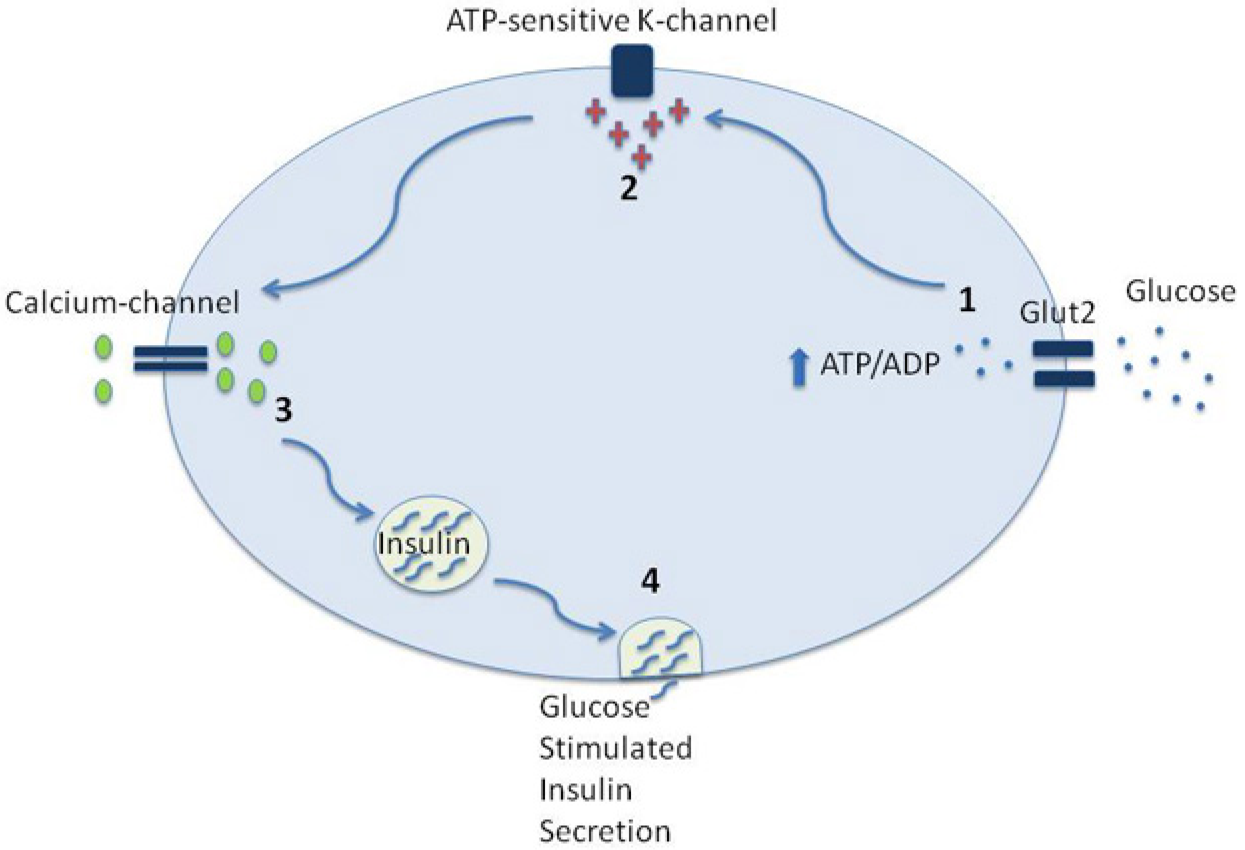
1. **Affinity** of receptors for signal molecules
   Often sub-nanomolar
2. **Cooperativity** in the interaction
   Small changes in ligand concentration results in large changes in receptor activation
3. **Amplification** of the signal
   Receptor is activated, which catalyzes the activation of many equivalents of a 2^{nd} enzyme….

Thyroid Hormones





Insulin and the Insulin Receptor

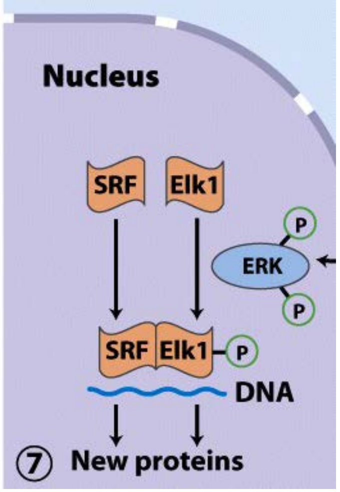


Insulin and the Insulin Receptor

Production stimulated by elevated blood glucose levels (synthesized in the pancreas)

Insulin

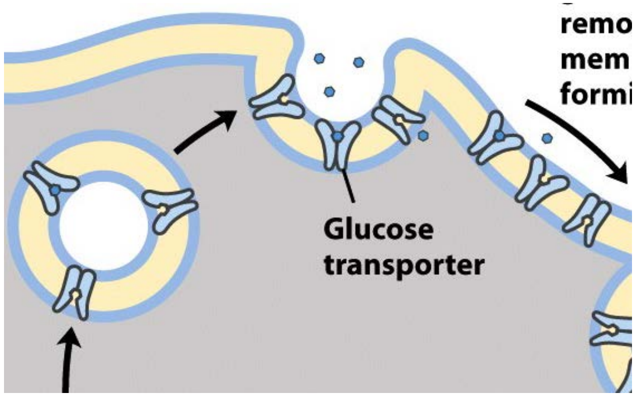
Cell division initiated

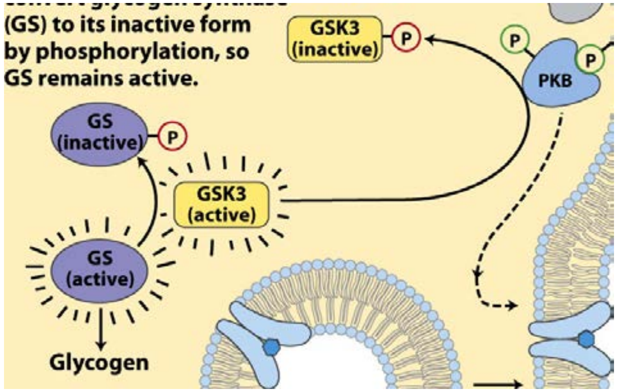


Sugar uptake into all cells via the Glucose Transporter

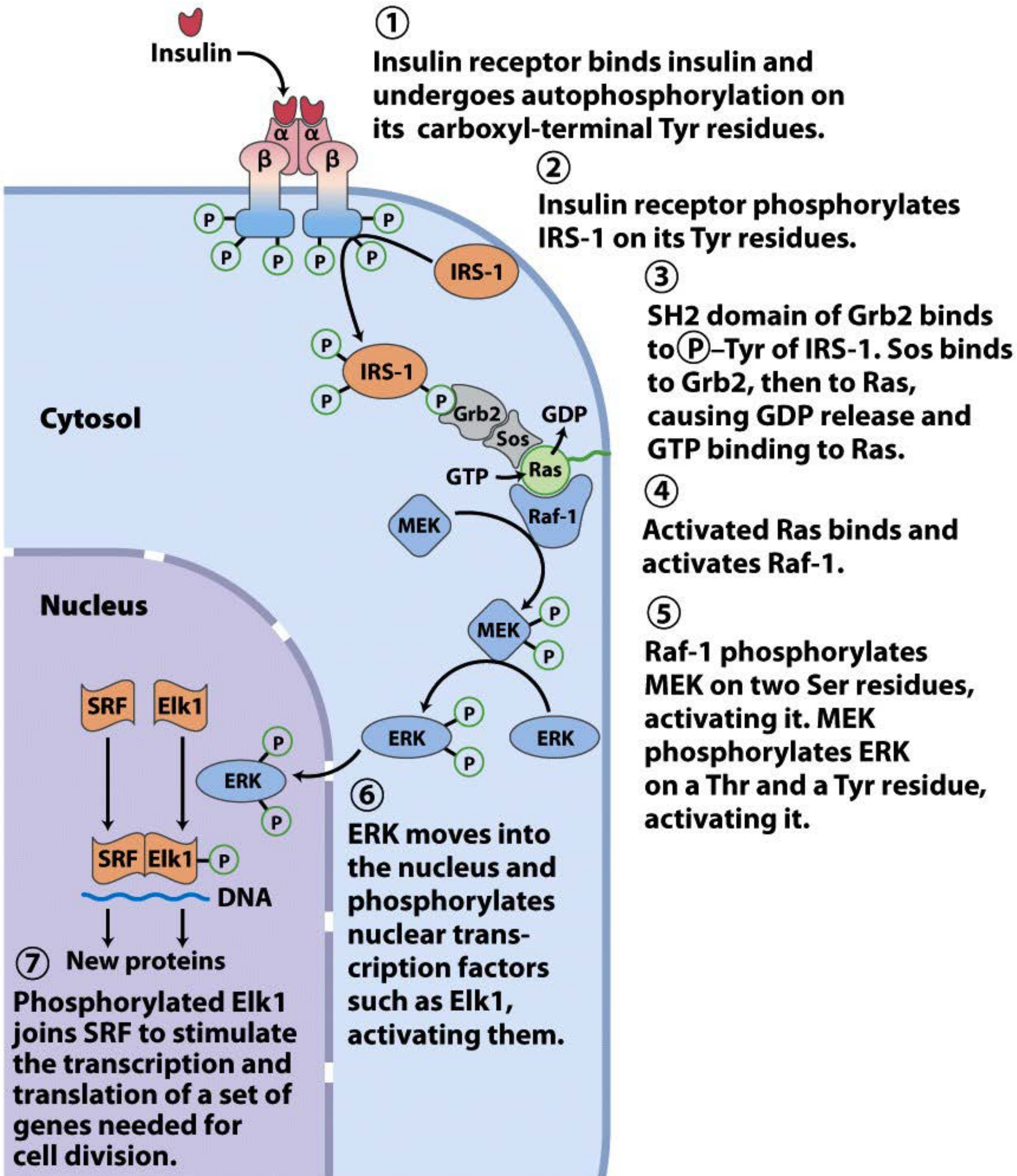
Glycogen synthesis is stimulated

Decreased Hunger

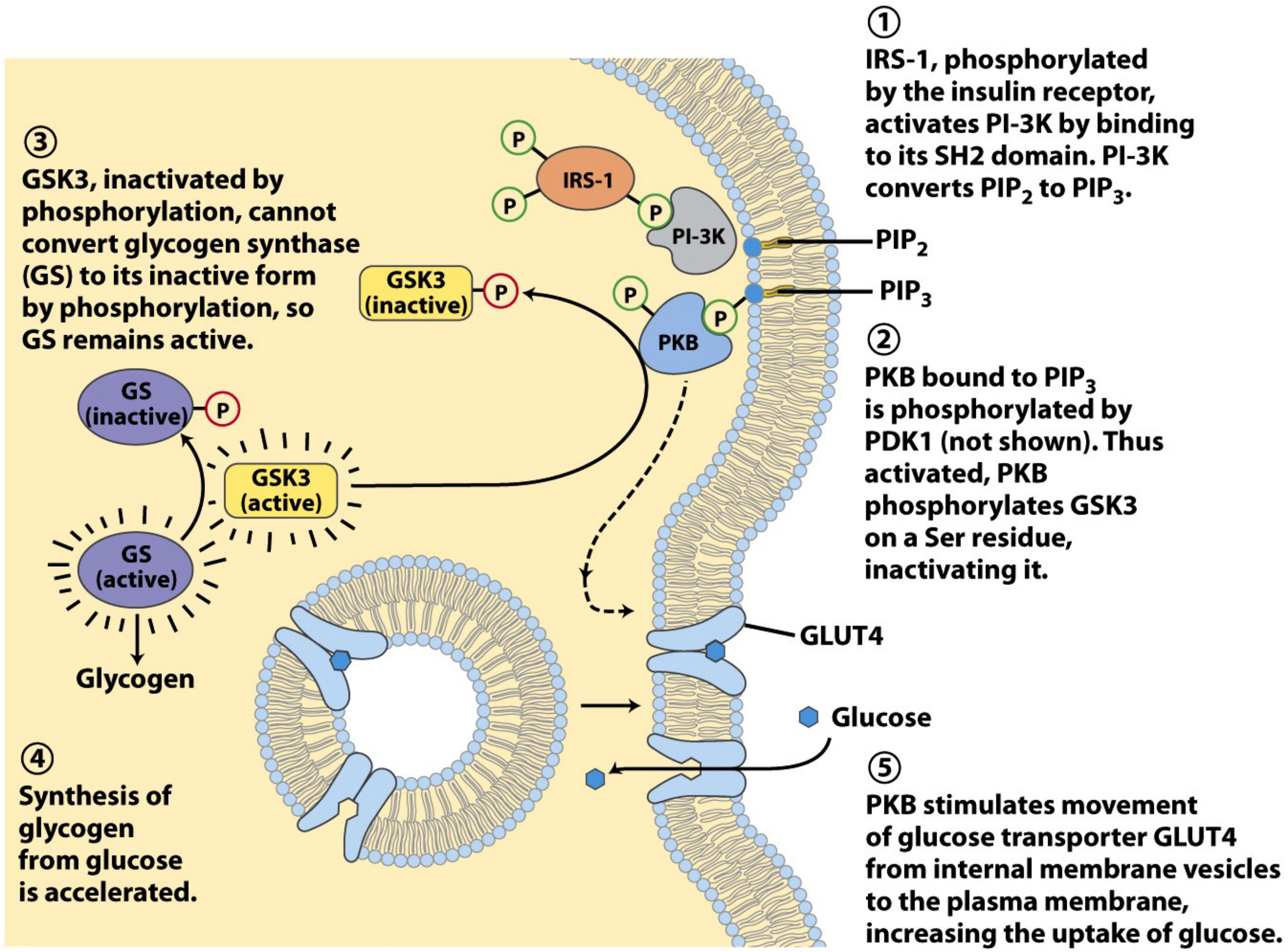


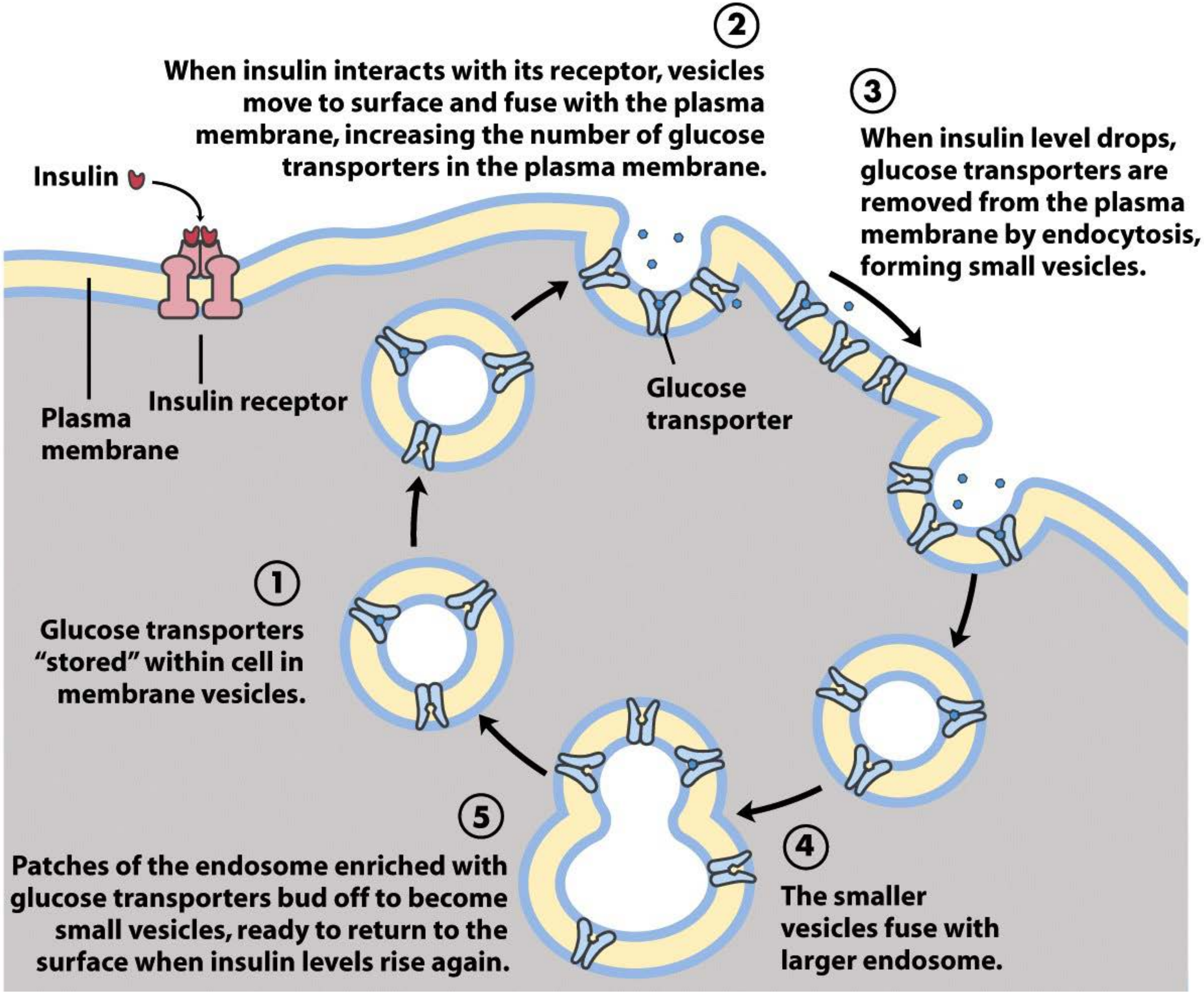


Insulin and the Insulin Receptor

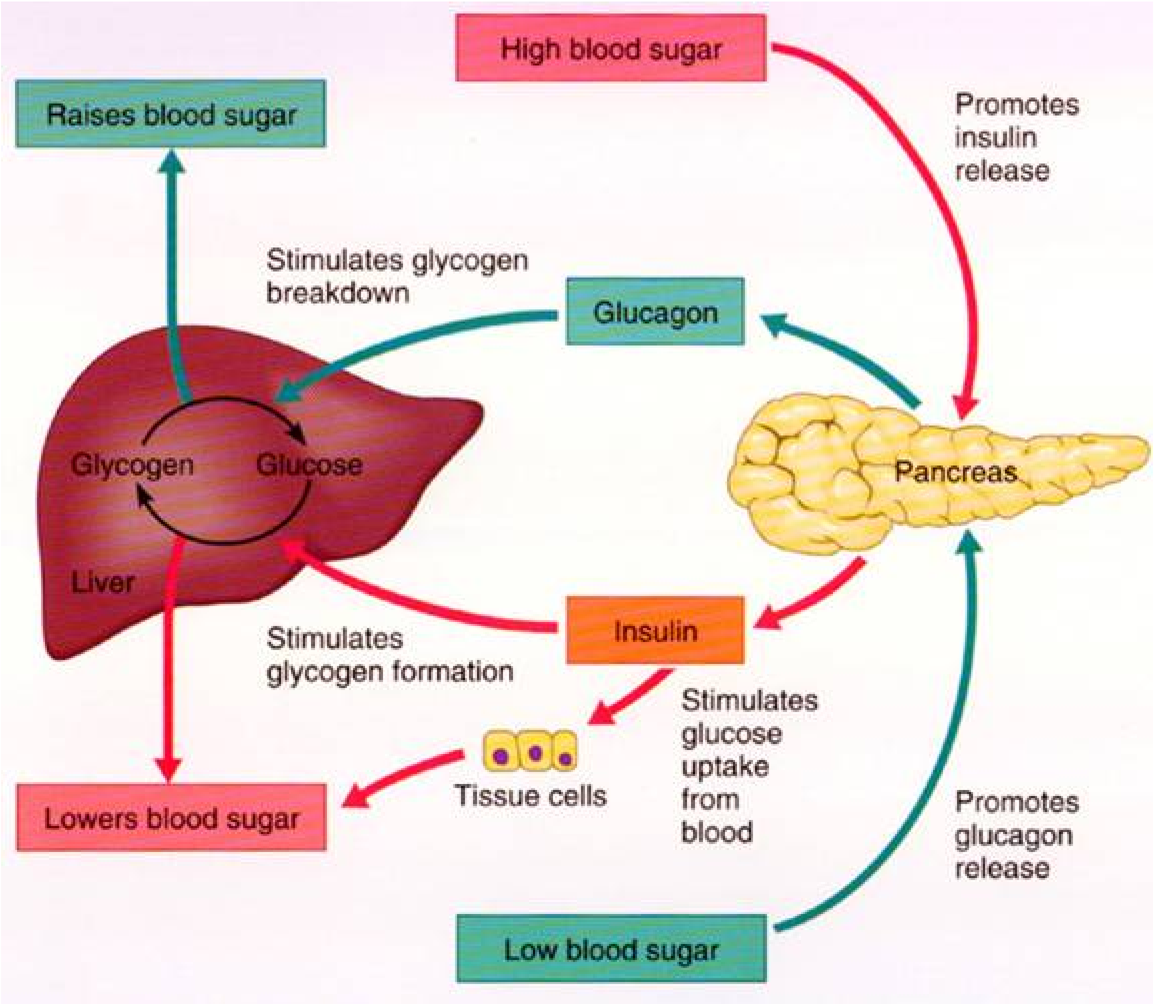


Insulin and the Insulin Receptor



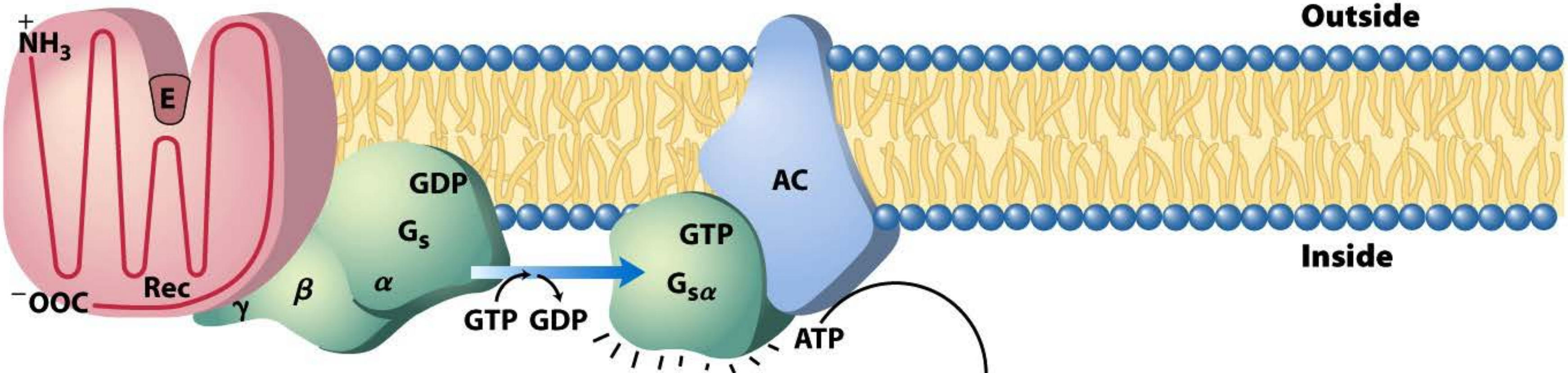

2
When insulin interacts with its receptor, vesicles move to surface and fuse with the plasma membrane, increasing the number of glucose transporters in the plasma membrane.
3
When insulin level drops, glucose transporters are removed from the plasma membrane by endocytosis, forming small vesicles.
Insulin
Plasma membrane
Insulin receptor
Glucose transporter
1
Glucose transporters "stored" within cell in membrane vesicles.
5
Patches of the endosome enriched with glucose transporters bud off to become small vesicles, ready to return to the surface when insulin levels rise again.
4
The smaller vesicles fuse with larger endosome.

The Physiological Response to Blood Sugar



Epinepherine Receptor Action (same as Glucagon)

① Epinephrine binds to its specific receptor.



② The occupied receptor causes replacement of the GDP bound to G_s by GTP, activating G_s.

③ G_s (α subunit) moves to adenylyl cyclase and activates it.

④ Adenylyl cyclase catalyzes the formation of cAMP.

cAMP

⑤ cAMP activates PKA. →

⑥ Phosphorylation of cellular proteins by PKA causes the cellular response to epinephrine.

cyclic nucleotide phosphodiesterase

5′-AMP

⑦ cAMP is degraded, reversing the activation of PKA.

Physiologic responses to epinephrine by organ

Organ	Effects
Heart	Increases heart rate
Lungs	Increases respiratory rate
Systemic	Vasoconstriction or vasodilation
Liver	Stimulates glycogenolysis
Systemic	Triggers lipolysis
Systemic	Muscle contraction

cAMP/PKA Regulated Genes

TABLE 12–2 Some Enzymes and Other Proteins Regulated by cAMP-Dependent Phosphorylation (by PKA)

Enzyme/protein	Sequence phosphorylated*	Pathway/process regulated
Glycogen synthase	RASCTSSS	Glycogen synthesis
Phosphorylase *b* kinase		
α subunit	VEFRRLSI	Glycogen breakdown
β subunit	RTKRSGSV	Glycogen breakdown
Pyruvate kinase (rat liver)	GVLRRASVAZL	Glycolysis
Pyruvate dehydrogenase complex (type L)	GYLRRASV	Pyruvate to acetyl-CoA
Hormone-sensitive lipase	PMRRSV	Triacylglycerol mobilization and fatty acid oxidation
Phosphofructokinase-2/fructose 2,6-bisphosphatase	LQRRRGSSIPQ	Glycolysis/gluconeogenesis
Tyrosine hydroxylase	FIGRRQSL	Synthesis of L-dopa, dopamine, norepinephrine, and epinephrine
Histone H1	AKRKASGPPVS	DNA condensation
Histone H2B	KKAKASRKESYSVYVYK	DNA condensation
Cardiac phospholamban (cardiac pump regulator)	AIRRAST	Intracellular [Ca^{2+}]
Protein phosphatase-1 inhibitor-1	IRRRRPTP	Protein dephosphorylation
PKA consensus sequence†	xR[RK]x[ST]B	Many