Phosphate Pentose Pathway

Enzyme	Reaction	Notes
Glucose-6-Phosphate Dehydrogenase	Glucose-6-phosphate + $NADP^+$ → NADPH + 6-phosphogluconolactone	Committed & rate-limiting step A high NADPH/NADP+ ratio **inhibits** G6PD. NADPH is a competitive inhibitor. Insulin **upregulates** the G6PD gene expression. <u>G6PD deficiency:</u> -hemolytic anemia -common; 200-400 million worldwide -highest prevalence in Middle East, southeast Asia, mediterranean -X-linked heritance– males are more affected -over 400 mutations -provides resistance to falciparum malaria (affects RBCs; anemia = no RBCs = no malaria) -neonatal jaundice
Gluconolactonase	6-phosphogluconolactone + H2O → 6-phosphogluconate + H^+	
6-Phosphogluconate Dehydrogenase	6-phosphogluconate + $NADP^+$ → NADPH + CO2 + Ribulose-5-phosphate	
Ribose-5-Phosphate Isomerase	Ribulose-5-phosphate ←→ Ribose-5-phosphate	
Epimerase	Ribose-5-phosphate ←→ Xylulose-5-phosphate	
Transketolase	Ribose-5-phosphate[2] + xylulose-5-phosphate ←→ G3P + Sedoheptulose-7-phosphate	
Transaldolase	G3P + Sedoheptulose-7-phosphate ←→ Erythrose-4-phosphate + fructose-6-phosphate[3]	

Transketolase	Erythrose-4-phosphate + Xylulose-5-phosphate ←→ G3P + fructose-6-phosphate	
Glutathione Peroxidase	2 G-SH (reduced) + H_2O_2 → 2 H_2O + GS–SG (oxidized)	Important in RBCs, which dont have the appropriate machinery (no organelles) to protect themselves from oxidative stress. Requires selenium
Glutathione Reductase	NADPH + H^+ + GS–SG (oxidized) → 2 G-SH (reduced) + $NADP^+$	Important in RBCs, which dont have the appropriate machinery (no organelles) to protect themselves from oxidative stress.
Superoxide Dismutase	2 O_2^- + 2 H^+ → O_2 + H_2O_2	
Catalase	2 H_2O_2 → O_2 + 2 H_2O	
Nitric Oxide Synthase	L-Arginine + NADPH → NADP+ + Nitric oxide *Coenzymes: MN, FAD, heme, tetrahydrobiopterin*	Has three isoforms Inducible Ca^{2+}-independent NO kills invading bacteria, decreases platelet aggregation, and is a vasodilator **NO mechanism of killing bacteria:** O_2 becomes O^-, which is then combined with NO to form $ONOO^-$ which kills the bacteria **NO mechanism of action in smooth muscle cells:** stimulation of GTP→ cGMP → protein kinase G → phosphorylation of Ca^{2+} channels → decrease calcium entry into smooth muscle cells → muscle relaxation & lowering of blood pressure

Metabolism of Lipids: Transport & Absorption

FA: fatty acid **CE**: cholesteryl ester **TAG**: triacylglycerol

Enzyme	Reaction	Notes
Lingual Lipase & Gastric Lipase	Hydrolyzes the ester bonds between fatty acids and glycerol molecules in TAGs	Acid-stable; optimum pH 2.5-5 No colipases or emulsifiers needed– short and medium chain FAs are relatively small and therefore have more polarity, which allows for gastric and lingual lipases to catalyze their hydrolysis without needing emulsifiers. Very crucial in infants due to their diets (breast milk) being high in short and medium chain FAs (<13C) Inhibited by long chain FAs Responsible for 30% of lipid hydrolysis
Pancreatic Lipase	Hydrolyzes long-chain fatty acids from TAGs Cleaves the **first** and **third** fatty acid chains from	Secreted in the small intestine. Requires colipases and emulsifiers (bile acids and salts). Responsible for ~70% of lipid hydrolysis
Colipases	Makes room for lipase to associate with long chain FAs due to bile salts completely covering them, preventing lipase attachment.	Secreted as zymogens, or **pro**enzymes, from the pancreas Activated by trypsin in the small intestine Lipase-colipase deficiency is considered an **orphan disease.**
Cholesterol Esterase	CE → Cholesterol + Fatty Acid	
Phospholipase A2	Phospholipid → Lysophospholipid + fatty acid (that was on carbon #2) *For example: phosphatidylcholine → lysophosphatidylcholine + cleaved C2 fatty acid*	Secreted as a zymogen, **pro**phospholipase A2. Activated by trypsin Requires bile salts
Lysophospholipase	Lysophospholipid → Glycerophosphoryl base + fatty acid (that was on carbon #1) *For example:* *Lysophosphatidylcholine →* *Glycerophosphorylcholine + cleaved C1 fatty acid*	Glycerophosphoryl base is excreted in feces, undergoes further degradation, or is absorbed.
Fatty Acyl CoA	Long chain FAs + CoA + ATP (synthetase) →	

Synthetase	Fatty acyl CoA (activated fatty acid)	
Acyl CoA:	Monoacylglycerol Acyltransferase: 2-Monoacylglycerol + fatty acyl CoA → Diacylglycerol + CoA **Not the final product**	Function: synthesis of TAGs & CEs (along with fat-soluble vitamins and apolipoprotein B-48) for the formation of chylomicrons to then be distributed to the lymphatic system. TAGs constitute the majority of chylomicrons.
	Diacylglycerol Acyltransferase: Diacylglycerol + fatty acyl CoA → Triacylglycerol + CoA	
	Cholesterol Acyltransferase: Cholesterol + fatty acyl CoA → Cholesteryl ester + CoA	
Lipoprotein Lipase	Hydrolyzes TAGs in chylomicrons (intestines → liver) & VLDLs (liver → peripheral tissues),	Projected from endothelial cells Affects lipoproteins as they are in circulation **Familial chylomicronemia (type I hyperlipoproteinemia):** rare, autosomal-recessive disorder caused by LPL or apoC-II (coenzyme) deficiency. This results in fasting chylomicronemia and severe hypertriacylglycerolemia, which may cause pancreatitis.
Cytidine Deaminase	apo-B gene CAA → UAA (stop codon)	mRNA transcripts that undergo deamination are cleaved earlier than ones that are unaffected, producing **apo-B48** protein in the **intestine**. **Apo-B100** protein is present in the **liver.**

Degradation of Fatty Acids

Enzyme	Reaction	Notes
Adipose Triglyceride Lipase (ATGL)	Hydrolyzes ester bonds in TAGs → 1 free fatty acid + diacylglycerol	Located in adipocytes
Hormone-Sensitive Lipase (HPL)	Hydrolyzes ester bond, only in **di**acylglycerols → 2 free fatty acids + monoacylglycerol	**Activated** by phosphorylation (glucagon/epinephrine) Enzyme present in adipocytes Requires hormonal actuation
Monoacylglycerol Lipase	Hydrolyze ester bonds in **mono**acylglycerols → 3 free fatty acids (2 previously) + glycerol	
AMP-Activated Kinase Kinases (AMPKK)	Unphosphorylated, inactive AMPK → active, phosphorylated AMPK	**Activated** by phosphorylation (glucagon/epinephrine)
Acetyl CoA Carboxylase (II)	Acetyl CoA + CO2 → Malonyl CoA (3C) *Carboxylation*	**Inhibited** by phosphorylation (glucagon/epinephrine), **activated** by dephosphorylation by **insulin**-induced phosphatase activity. ACC2, an isoform, regulates fatty acid oxidation in muscle cells, which lack ACC1 responsible for fatty acid synthesis.
Glycerol Kinase	Glycerol → Glycerol-3-Phosphate *Phosphorylation*	
Glycerol-3-Phosphate Dehydrogenase	G3P → DHAP *Oxidation*	DHAP is then used for gluconeogenesis
Thiokinase (Acyl CoA Synthetase)	Fatty acid + CoA + ATP → Fatty acyl CoA + AMP + PPi	
Carnitine Palmitoyltransferase I	Replaces the CoA in long chain FAs w/ carnitine, a necessary step for transport into the mitochondrial matrix, where oxidation occurs. LCFA-CoA + carnitine → LCFA-carnitine + free CoA	Present in the OMM Deficiency results in severe hypoglycemia, coma, and death– *cells cannot resort to fatty acids for energy due to the inability of FAs to bind to carnitine for transport.*

Carnitine Palmitoyltransferase II	Replaces the carnitine in long chain FAs w/ CoA, a necessary step for oxidation. LCFA-carnitine + free CoA→ LCFA-CoA + carnitine	Present in the IMM Inhibited by malonyl CoA– crucial molecule for fatty acid synthesis. Ensures that fatty acids that are freshly synthesized can't enter the matrix to be degraded. Deficiency results in severe hypoglycemia, coma, and death– *cells cannot resort to fatty acids for energy due to the inability of FAs to exchange carnitine for CoA to begin oxidation.*
Translocase	Transports LCFA-carnitine into the mitochondrial matrix, as well as transport the free carnitine back to the IMM space.	Mutation would cause carnitine deficiency especially in cardiac & skeletal muscle cells.
Acetyl CoA Carboxylase I	Used in fatty acid synthesis	97% of carnitine is present in skeletal and cardiac muscle cells, where there is no ACCI, thus, no FA synthesis. Skeletal muscles do contain ACCII to regulate FA degradation.
Acyl CoA Dehydrogenase *LCFAs*	Fatty acyl CoA + FAD → FADH2 + Enoyl CoA (double bond) *Oxidation*	FADH can be used in the ETC An isozyme of fatty acyl CoA dehydrogenase, medium chain FAs, deficiency is: • An autosomal-recessive disorder • Most common inborn error of β-oxidation (1:14,000 births worldwide) • Higher incidence among Caucasians of Northern European descent • Decreased ability to oxidize MCFAs (lack of energy) • Severe hypoglycemia and hypoketonemia • Treatment: avoidance of fasting Regular and frequent meals and snacks Diet high in carbohydrates and low in fat
Enoyl CoA Hydratase *LCFAs*	Enoyl CoA + H2O → 3-Hydroxyacyl CoA *Hydration*	
3-Hydroxyacyl CoA Dehydrogenase *LCFAs*	3-Hydroxyacyl CoA + NAD^+ → 3-Ketoacyl CoA + NADH *Oxidation*	NADH can be used in the ETC
Thiolase *LCFAs*	3-Ketoacyl CoA + CoA → Fatty acyl CoA + Acetyl CoA *Thiolytic cleavage*	Inhibited by high [acetyl CoA]s *Depleted supply of free CoA*

ODD-NUMBERED Propionyl CoA Carboxylase	Propionyl CoA + ATP + CO_2 → D-methylmalonyl CoA + ADP	Requires **biotin, & ATP**
Methylmalonyl CoA Epimerase	D-methylmalonyl CoA → L-methylmalonyl CoA	
Methylmalonyl CoA Mutase	L-methylmalonyl CoA → Succinyl CoA	Requires **coenzyme B12** Vitamin B12 deficiency or inactivation causes metabolic acidosis and neurological manifestations Succinyl CoA goes on to participate in Krebs cycle
MONOUNSATURATED Enoyl-CoA Isomerase	Shifts double bond from the 3,4 carbon position to the 2,3. The 2,3 position falls right at the beta oxidation site. Shifts double bond at the cleavage site from *cis* → *trans* position.	Since the double bond is already present, the first step of β-oxidation (oxidation of fatty acyl CoA to enoyl CoA) will not occur. Therefore, no FADH2 results from this step– loss of electrons.
POLYUNSATURATED 2,4-Dienoyl CoA Reductase	Reduces 2 double bonds to a single double bond at the site of cleavage.	NADPH-dependent → loss of electrons. Due to the presence of multiple double bonds, the loss of electrons is greater.
PEROXISOMAL β-OXIDATION FAD-Containing Acyl CoA Oxidase	Activated very long chain fatty acid + FAD → FADH2 + Enoyl CoA The equivalent of acyl CoA dehydrogenase in mitochondria **except for** FADH2 + O2 → FAD + H2O2 *loss of electrons*	VLCFAs are transported into the peroxisome in their inactive state by the ABC D class transporter. Once inside the peroxisome, their activation takes place. The remaining steps (hydration, oxidation, and cleavage) are catalyzed by the same enzymes in mitochondria except theyre **bifunctional proteins** instead of **trifunctional proteins** as they are in mitochondria. <u>Deficiencies:</u> - Zellweger Syndrome: dysfunctional peroxisome synthesis - X-linked adrenoleukodystrophy: dysfunctional peroxisomal transport– ABC class D transporters → VLCFA accumulation.
PEROXISOMAL *α*-OXIDATION Very Long Chain Fatty Acyl CoA Synthetase	Phytanic acid → Phytanic acid CoA (activated)	Outside the peroxisome
Phytanoyl CoA *α* Hydrolase	Phytanoyl CoA + OH → 2-hydroxyphytanoyl CoA	Used to breakdown branched fatty acids. Phytanic acid is a product of chlorophyll breakdown. Deficiency in PhyH causes **Refsum disease–** autosomal recessive.

2-Hydroxyphytanoyl CoA α Lyase	2-hydroxyphytanoyl CoA → pristanal + formyl CoA Formyl CoA → formic acid → CO2	Could produce formyl CoA, acetyl CoA, propionyl CoA, or methylpropionyl CoA
Aldehyde Dehydrogenase	Pristanal + NAD+ → NADH + pristanic acid	Cycle repeats until the entirety of the branch is oxidized.
ω-OXIDATION IN SER Mixed Function Oxidase	OH at ω- carbon of FA → fatty ω-hydroxyacid (alcohol)	Minor pathway Upregulated in MCAD which allows for cleavage of fatty acid from the omega carbon.
Alcohol Dehydrogenase	fatty ω-hydroxyacid (alcohol) + NAD+ → NADH + fatty ω-aldoacid	
Aldehyde Dehydrogenase	fatty ω-aldoacid + NAD+ → NADH + dicarboxylic acid	

Synthesis of Fatty Acids

Enzyme	Reaction	Notes
ATP Citrate Lyase	Citrate → OAA + acetyl CoA	Since this pathway occurs in the well-fed state, ATP is abundant. ATP inhibits isocitrate dehydrogenase which leads to citrate being transported from the mitochondria to the cytoplasm.
Acetyl CoA Carboxylase	Acetyl CoA + $HCO3^-$ + ATP → Malonyl CoA + ADP *Coenzyme: vitamin B7- biotin*	Rate-limiting step ACC and biotin are covalently linked. **Activated by** high [citrate]s which stimulate its polymerization from inactive promoters, and by insulin-induced phosphatase activity (AMPK and ChREBP), and insulin activating tyrosine kinase receptors, activating SREBPc1). **Inhibited by** palmitoyl CoA (feedback inhibition) and glucagon/epinephrine (phosphorylation of AMPK and ChREBP). **Metformin** (glucophage) is a medication used to monitor glucose levels in diabetic patients by mimicking fasting state mechanism– phosphorylation AMPK, phosphorylating ChREBP and inactive SREBP. It also mediates glucose uptake from the bloodstream and inhibits gluconeogenesis.
Fatty Acid Synthase	Fatty acid synthesis	Homodimeric complex composed of 6 enzymatic domains and a binding domain for acyl carrier protein (14 active sites in total).
Phosphopantetheine	Carries acyl units on its terminal thiol group and presents them to the catalytic domains of FAS.	Derivative of pantothenic acid (vitamin B5) Component of CoA
Malonyl/Acetyl CoA-ACP Transacylase	Transfers acyl group to the ACP by the reactive -SH group.	
3-Ketoacyl-ACP Synthase	Transfers acyl group from ACP to cysteine to leave ACP free to bind malonyl CoA.	Condensing enzyme
Malonyl/Acetyl CoA-ACP Transacylase	Adds malonyl CoA (COO- from ACC + acetyl CoA) to the ACP.	
3-Ketoacyl-ACP Synthase	Removes a CO2 molecule from malonyl CoA, acetyl CoA (2 carbons) then joins the remains of malonyl CoA (2 carbons) on ACP.	Condensing enzyme 4-carbon molecule attached to ACP.

3-Ketoacyl ACP Reductase	S-CO-CH2-**CO**-CH3 + NADPH → S-CO-CH2-**CHOH**-CH3 + $NADP^+$	Reduction of the double bond on the second carbonyl to produce an alcohol.
3-Hydroxyacyl-ACP Dehydratase	S-CO-CH2-**CHOH**-CH3 → H2O + S-CO-**CH=CH**-CH3	Got rid of the alcohol group.
Enoyl-ACP Reductase	S-CO-**CH=CH**-CH3 + NADPH → $NADP^+$ + S-CO-CH2-CH2-CH3	Produces a saturated fatty acid with a terminal carbonyl group. The saturated 4-carbon fatty acid is then transported to the cysteine residue, leaving the ACP free to bind another malonyl CoA to lengthen the fatty acid chain. The previous steps repeat until the desired fatty acid chain length is acquired. Each cycle adds 2 carbons to the chain. In lactating mammary glands terminate chain elongation early. Elongation of fatty acids (such as palmitate 16C) up to 18-20 carbons takes place in the **SER**, without ACP or FAS. **NADPH** is the source of **electrons**, while **malonyl CoA** is the 2 **carbon** donor. Further elongation to produce VLCFAs takes place in the **brain**, more specifically in the **mitochondria**. **NADPH** and **NADH** are sources of **electrons**, and **acetyl CoA** is the source of **carbon**. Production of VLCFA will not start from scratch, and will elongate medium chain fatty acids or shorter.
Thioesterase	Addition of H2O to the fatty acid attached to ACP, releasing the fatty acid from FAS.	
Fatty Acyl CoA Desaturase	Introduces double bonds on carbons 4, 5, 6, and 9. First double bond is inserted between C9 and C10 → oleate (18:1), and palmitoleic acid (16:1) Saturated fatty acid + NADH → Monounsaturated fatty acid + NAD^+	Due to the limited number of desaturases in human cells, fatty acids with double bonds beyond the 10th carbon cannot be synthesized in the body. Rather, they are obtained from diet, such as linoleic and linolenic acids. **Electron source:** NADH **Electron acceptor:** O2, cytochrome B5 and its linked FAD reductase. **Location:** SER **Substrate:** long chain fatty acids.

Metabolism of Glycerophospholipids

Enzyme	Reaction	Synthesizes
Acyltransferases	Glycerol-3-phosphate + fatty acid-CoA → lysophosphatidic acid	Phosphatidic acid (steps 1, 2, and 4)
	Lysophosphatidic acid + fatty acid-CoA → phosphatidic acid	
	Diacylglycerol + fatty acid-CoA → triacylglycerol	
Phosphatase	Phosphatidic acid → diacylglycerol	Phosphatidic acid (step #3)
CTP-Phosphocholine Cytidylyltransferase	Phosphocholine → CDP-choline	Phosphatidylcholine
CDP-Choline: Diacylglycerol Choline Phosphotransferase	CDP-choline + DAG → Phosphatidylcholine + CMP	Phosphatidylcholine
Phosphatidylethanolamine N-Methyltransferase	Phosphatidylethanolamine + CH3 (from SAM) → phosphatidylcholine Uses folic acid (vitamin B9)	Phosphatidylcholine
Phosphatidylserine Decarboxylase	PS - CO2 → Ph-ethanolamine	Phosphatidylethanolamine
Phosphatidylserine Synthase	PS + ethanolamine ←→ PE + serine	Phosphatidylserine/ethanolamine/choline
	PS + choline ←→ PC + serine	
Phosphatidylinositol Synthase	Inositol + CDP-DAG → Phosphatidylinositol + CMP	Phosphatidylinositol - An arachidonate reservoir - Produces signaling molecules when phospholipase C is cleaved.

Cardiolipin Synthase	CDP-DAG + Phosphatidylglycerol → Cardiolipin + CMP	Cardiolipin (two phosphatidylglycerol connected by a phosphate group)
Phospholipase A2	Removes fatty acids at carbon #2	Present in many mammalian tissues and pancreatic juice, pancreatic secretions contain the proenzyme, activated by **trypsin** and requires **bile salts** for activity. Present in snake and bee venoms. Works on phosphatidylinositol, releasing arachidonic acid. Inhibited by glucocorticoids.
Phospholipase A1	Removes fatty acids at carbon #1	Present in many mammalian tissues
Phospholipase C	Removes the head group + Pi	Liver lysosomes Activated by PIP2, produces second messengers
Phospholipase D	Removes head group → Phosphatidic acid	

Plasmalogens:

- Phosphatid**a**lethanolamine: similar structure to phosphatidylethanolamine except for ether linkage. Abundant in nerve tissue.
- Phosphatid**a**lcholine: Abundant in cardiac muscle cells.
- Platelet-activating factor: has a saturated alkyl group in an ether link to carbon 1 and an acetyl residue at carbon 2. Prothrombotic and inflammatory factors.

Metabolism of Sphingolipids

Enzyme	Reaction	Notes
Pyridoxal Phosphate	Palmitoyl CoA + Serine + NADPH → Sphinganine + CoA + CO_2 + $NADP^+$ *Condensation*	
Sphingomyelinase	Hydrolyzes sphingomyelin to sphingosine + phosphorylcholine	Type of phospholipase C (cleaves head group + phosphate)
Ceramidase	Ceramide → Sphingosine + free fatty acid	Sphingosine and ceramide regulate signal transduction pathways by influencing activity of protein kinase C, as well as promoting apoptosis.
Glycosyltransferases	UDP-sugars + ceramide→ glycosphingolipids	
Sulfotransferase	PAPS + galactocerebroside → galactocerebroside sulfate	
Lysosomal Hydrolases	Remove sugars in glycosphingolipids sequentially starting with the last one added.	Defect in glycoprotein, GAG, or glycosphingolipids hydrolysis is deemed a lysosomal storage disease.
Sialidase (Neuraminidase)	Glycosidase that removes sialic acid during ganglioside degradation.	

Deficient Enzyme	Associated Disease
Sphingomyelinase	Niemann-Pick Disease - Enlarged liver and spleen filled with lipids - Severe intellectual disability and neurodegeneration as well as death in early childhood (type A) - Type A is more severe than type B, and is more frequent in Ashkenazi Jews

	- Autosomal recessive
Hexosaminidase A	Tay-Sachs Disease - Accumulation of GM2 gangliosides - Neurodegenearation - Blindness, seizures - Muscle weakness - Autosomal recessive - Bulging lysosomes
Glucosidase	Gaucher Disease - Autosomal recessive - Most common lysosomal storage disorder - Accumulation of glucocerebrosides - ERT (enzyme replacement therapy) is available - Bone marrow transplantation - Substrate reduction therapy
Ceramidase	Farber Disease - X-linked - Accumulation of ceramide - Painful and progressive joint deformity - Hoarse cry - Tissue granulomas - ERT available

Ketogenesis

Enzyme	Reaction	Notes
Thiolase	3-Ketoacyl CoA + CoA → Acetyl CoA + Fatty acyl CoA (in hepatocytes)	
	2 Acetyl CoAs → Acetoacetyl CoA + CoA (in hepatocytes)	
	Acetoacetyl CoA → 2 Acetyl CoAs (in peripheral tissues)	
HMG CoA Synthase	Acetoacetyl CoA + Acetyl CoA → HMG CoA + CoA	Rate-limiting step This enzyme is present in the mitochondria of hepatocytes.
HMG CoA Lyase	HMG CoA → Acetoacetate + Acetyl CoA	
3-Hydroxybutyrate Dehydrogenase	Acetoacetate + NADH → NAD^+ + 3-hydroxybutyrate (in hepatocytes)	Remember that the increased NADH/NAD^+ ratio suppresses gluconeogenesis.
	3-hydroxybutyrate + NAD^+ → NADH + acetoacetate (in peripheral tissues)	
Thiophorase	Acetoacetate + Succinyl CoA → Acetoacetyl CoA + Succinate	Not present in the liver

Metabolism of Cholesterol

Enzyme	Reaction	Notes
HMG CoA Synthase	2 Acetyl CoA → **Acetoacetyl CoA → HMG CoA** *Similar steps to ketogenesis.*	Enzyme is present in the cytosol of hepatocytes
HMG CoA Reductase	HMG CoA + 2 NADPH → 2 $NADP^+$ + CoA + Melanovate	Committed & rate-limiting step Integral membrane protein in SER membrane with its catalytic domain projecting towards the cytosol. **Inhibited by** phosphorylation by glucagon/epinephrine, binding SCAP & INSIG to SREBP-2, high [cholesterol], statins. **Activated by** insulin (phosphatases → dephosphorylate AMPK → active SREBP-2)
Kinases	Melanovate + 2 ATP → 2 ADP + 5-pyrophospphomelanovate	Activates melanovate after it is transported to the peroxisome.
Decarboxylase	5-pyrophosphomelanovate + ATP → CO2 + IPP + ADP + Pi	Phosphate group from ATP is for energy, not phosphorylation.
Isomerase	IPP (5C) → DPP (5C)	Transfers double bond from C1 & 2 to C2 & 3
Synthase	IPP (repeat previous steps to form another IPP) + DPP → GPP + PPi (10C)	Farnesyl covalently linking to proteins is known as **prenylation** which is used to anchor protein to the cytosolic side of the plasma membrane.
	GPP + IPP (3rd molecule) → FPP (15C) + PPi	
Squalene Synthase	2 FPP + NADPH → PPi + $NADP^+$ + squalene (30C)	Squalene is a linear molecule that undergoes cyclization in the SER.
Squalene Monooxygenase	Takes a single O atom and adds it as OH to squalene and oxidizes NADPH. The other oxygen atom is reduced to H2O.	

Lanosterol Synthase	Squalene → Lanosterol *Cyclization*	
No enzyme mentioned	Lanosterol + O2 + NADPH → Cholesterol + $NADP^+$	
Acyl CoA Cholesterol Acyltransferase	Fatty acyl CoA + Cholesterol → Cholesteryl ester	Esterification in the cells
Lecithin Acyl CoA Cholesterol Acyltransferase	Lecithin + Cholesterol → Cholesteryl ester + lysolecithin	Esterification in the plasma
7-α-Cholesterol Hydroxylase	Cholesterol + O2 + NADPH→ 7-Hydroxycholesterol + $NADP^+$ One oxygen atom is used to add to cholesterol, while the other is reduced to H2O	Rate-limiting step Bile acid Inhibited by bile acids Enzyme is an SER-associated P450 monooxygenase that's only found in the **liver.**

Metabolism of Eicosanoids

Enzyme	Reaction	Notes
Prostaglandin H2 Synthase	Cyclooxygenase: Incorporates an oxygen into PGG2 structure → cyclization	COX has two isoforms: 1) COX-1: constitutively active, platelet aggregation, gastric renal tissue, homeostasis. 2) COX-2: inducible, inflammation, bacterial infections. Both can synthesize PGH2. Inhibition of COX-2 can be overcome in endothelial cells, whereas COX-1 inhibition by aspirin cannot be overcome in platelets. Small doses of aspirin can reduce the risk of thrombus formation.
	Peroxidase: Uses glutathione and acts on the peroxide group in PGG2. GSH → GS-SG	
Thromboxane Synthase	PGH2 → TXA	Induces platelet aggregation and vasoconstriction. Present in platelets.
Prostacyclin Synthase	PGH2 → PGI2	Inhibits platelet aggregation and causes vasodilation. Present in endothelial cells.
5-Lipoxygenase	Arachidonic Acid → 5-HPETE	NSAIDs like aspirin have no inhibitory effect on 5-lipoxygenase. They only function on cyclooxygenases. Cortisol can inhibit 5-lipoxygenase, which reduces leukotriene synthesis.
_	5-HPETE → Leukotrienes A4 Uses glutathione.	LTs are produced in various tissues, such as leukocytes, mast cells, platelets, cardiac cells. LTA4 LTB4 *by LTA4 hydrolase* LTC4 *removal of glutamate from LTA4, by LTC4 synthase.* LTD4 *removal of glycine form LTC4* LTF4 *addition of another glutamate*