De Novo Synthesis of Palmitic Acid

This presentation explores how palmitic acid is synthesized in the body.

We will cover key enzymes, regulation, and clinical implications.

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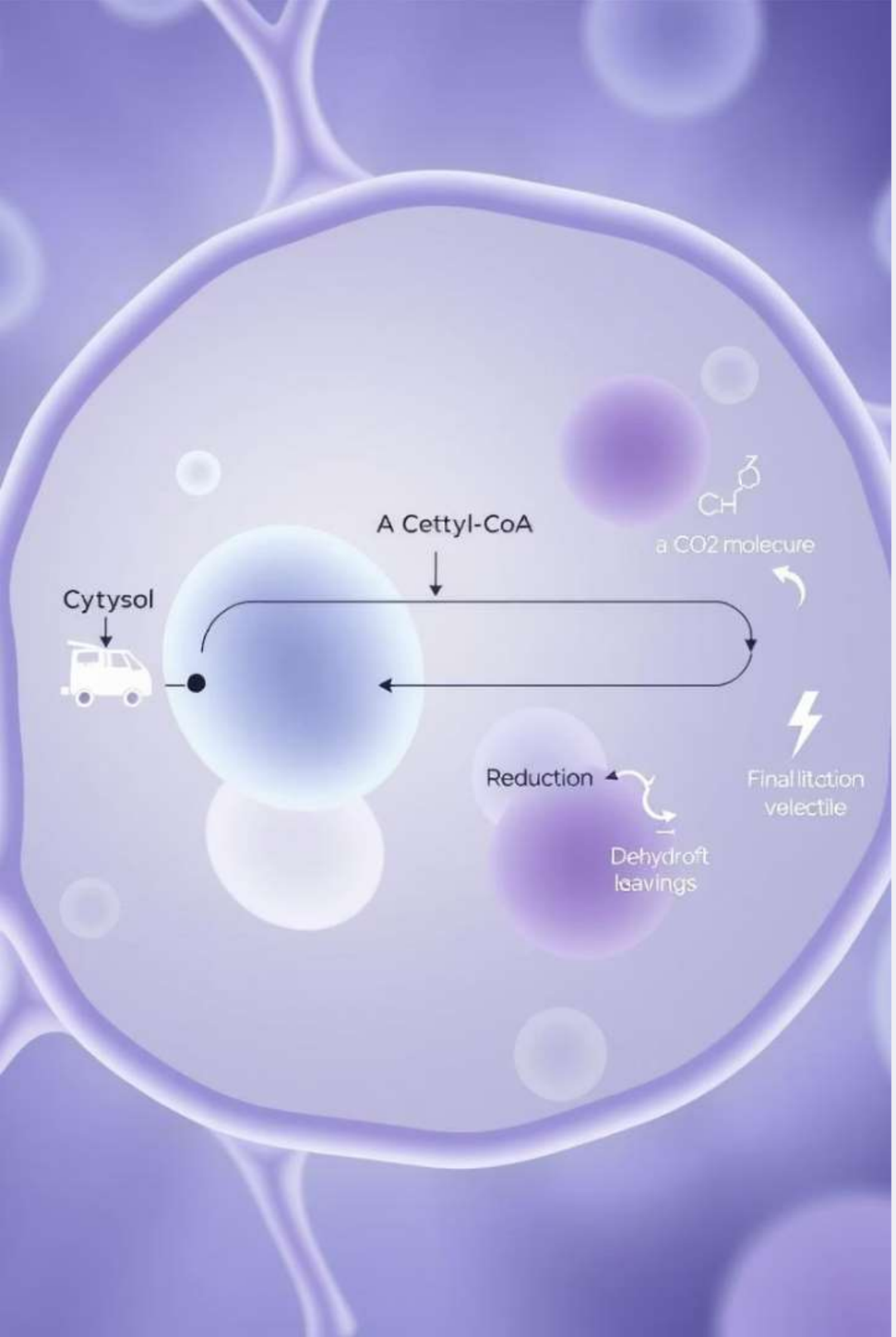


Introduction to Fatty Acid Synthesis

De Novo Synthesis

Creation of fatty acids from acetyl-CoA in cytosol.

Major Sites

Liver, adipose tissue, and lactating mammary glands.

Primary Product

Palmitic acid (16 carbons, fully saturated).

Key Precursors

Acetyl-CoA

Produced in mitochondria and transported via citrate shuttle.

NADPH

Provides reducing power, mainly from pentose phosphate pathway.

ATP

Energy currency fueling fatty acid synthesis steps.

Acetyl-CoA Carboxylase (ACC)

Committed Step

ACC converts acetyl-CoA to malonyl-CoA using biotin.

Isoforms

ACC1 in cytosol; ACC2 in mitochondria.

Regulation

Citrate activates; palmitoyl-CoA inhibits ACC activity.

Fatty Acid Synthase (FAS) Complex

Multifunctional

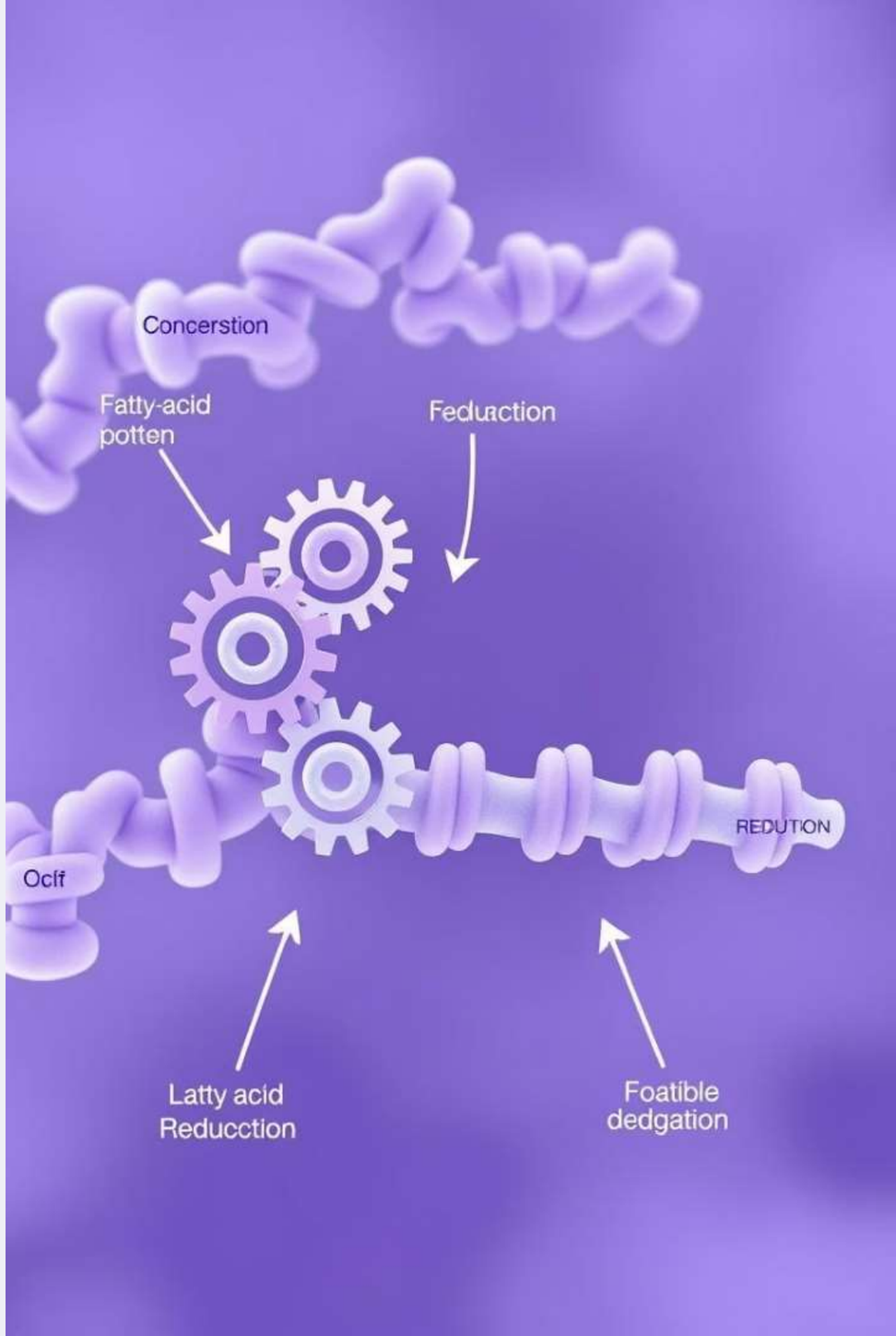
Contains seven enzymatic activities.

Acyl Carrier Protein

Holds growing fatty acid chain via phosphopantetheine.

Stepwise Addition

Adds two-carbon units from malonyl-CoA sequentially.



FAS Catalytic Mechanism

1

Condensation

Acetyl-CoA and malonyl-CoA form carbon chain, releasing CO2.

2

Reduction

NADPH reduces keto group to hydroxyl.

3

Dehydration & Reduction

Removes water and reduces double bond, repeating until 16 carbons.

Regulation of Fatty Acid Synthesis

1

Insulin

Activates synthesis by boosting ACC activity.

2

Glucagon & Epinephrine

Inhibit synthesis by inactivating ACC.

3

Metabolic Feedback

Citrate activates; palmitoyl-CoA inhibits fatty acid synthesis.

4

Diet Effects

High fat decreases, high carb increases synthesis.

Clinical Significance

Cancer

FAS is often upregulated, aiding tumor growth.

Metabolic Disorders

ACC deficiencies and fatty liver disease linked to dysfunction.

Pharmaceuticals

FAS inhibitors being studied as cancer therapies.

Stearoyl-CoA Desaturase

Converts stearic acid to oleic acid, impacting fat composition.