Metabolomics Overview

Targeted vs Untargeted

- Targeted: quantify specific metabolites
- Untargeted: broad metabolite profiling
- Semi-targeted approaches

Primary Metabolites

- Central metabolism (glycolysis, TCA)
- Amino acids, nucleotides
- Energy production molecules

Secondary Metabolites

- Plant natural products
- Signaling molecules
- Defense compounds

Metabolic Flux

- Dynamic metabolite changes
- Isotope tracing (13C, 15N)
- Pathway activity measurement

1. Targeted vs Untargeted Metabolomics

Targeted Metabolomics

Focused analysis of predefined metabolites with high precision and accuracy.

- **Advantages:** High sensitivity, excellent quantification, validated methods
- **Applications:** Clinical diagnostics, biomarker validation, quality control
- **Examples:** Glucose monitoring, amino acid panels, fatty acid profiling

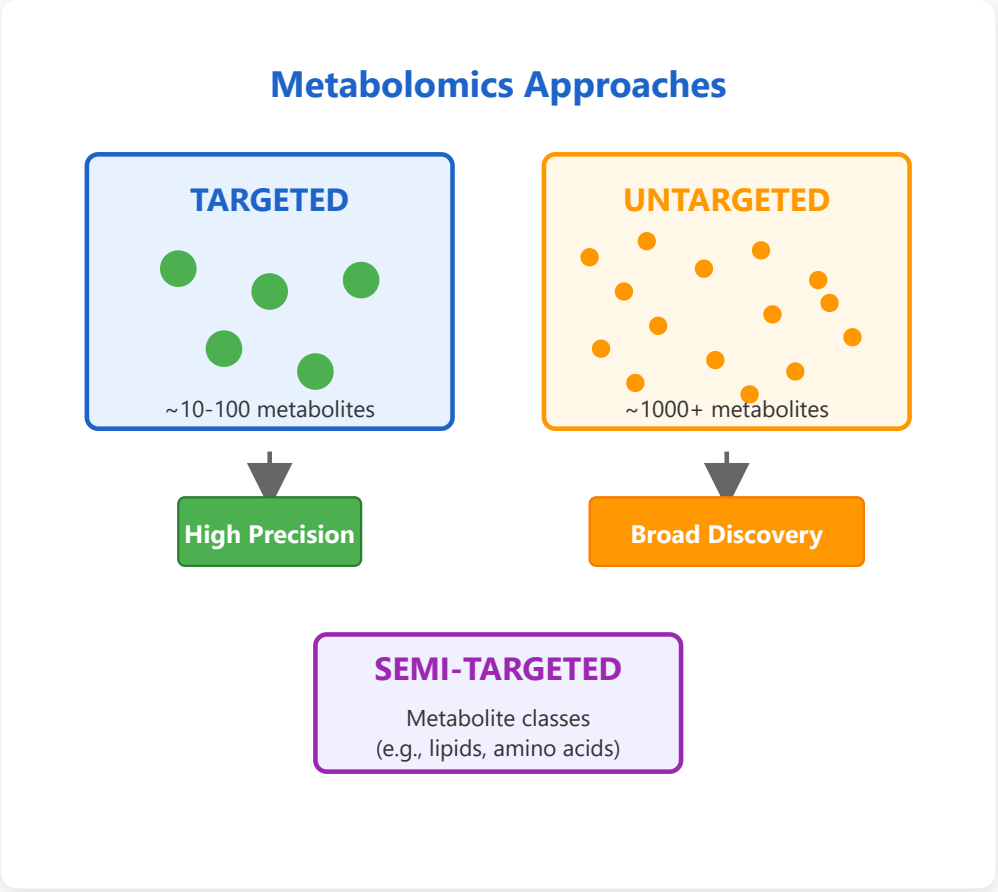
Untargeted Metabolomics

Comprehensive profiling to detect as many metabolites as possible without bias.

- **Advantages:** Discovery-driven, detects unexpected changes, holistic view
- **Applications:** Biomarker discovery, pathway analysis, systems biology
- **Challenges:** Identification complexity, data processing requirements

Semi-Targeted Approaches

Balance between coverage and quantification, focusing on metabolite classes.



2. Primary Metabolites

Definition

Essential molecules directly involved in normal growth, development, and reproduction. These are fundamental for cellular function and energy production.

Central Metabolism

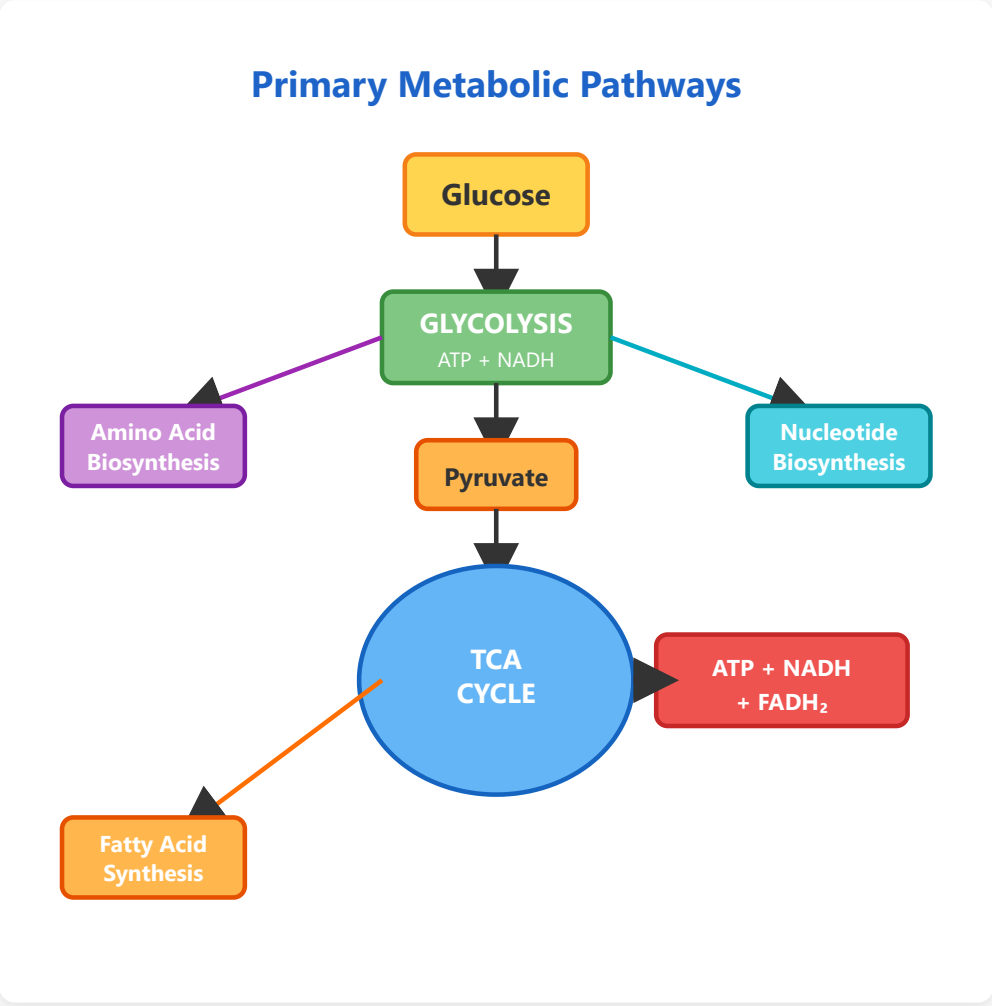
- **Glycolysis:** Glucose breakdown to pyruvate, producing ATP and NADH
- **TCA Cycle:** Complete oxidation of acetyl-CoA, generating energy carriers
- **Pentose Phosphate Pathway:** NADPH and ribose-5-phosphate production

Building Blocks

- **Amino Acids:** 20 standard amino acids for protein synthesis
- **Nucleotides:** DNA/RNA components (ATP, GTP, CTP, UTP)
- **Fatty Acids:** Membrane lipids and energy storage

Clinical Significance

Alterations in primary metabolites indicate metabolic disorders, diabetes, cancer metabolism, and nutritional deficiencies.



3. Secondary Metabolites

Definition

Specialized compounds not directly involved in growth but crucial for ecological interactions, defense, and organism survival in specific environments.

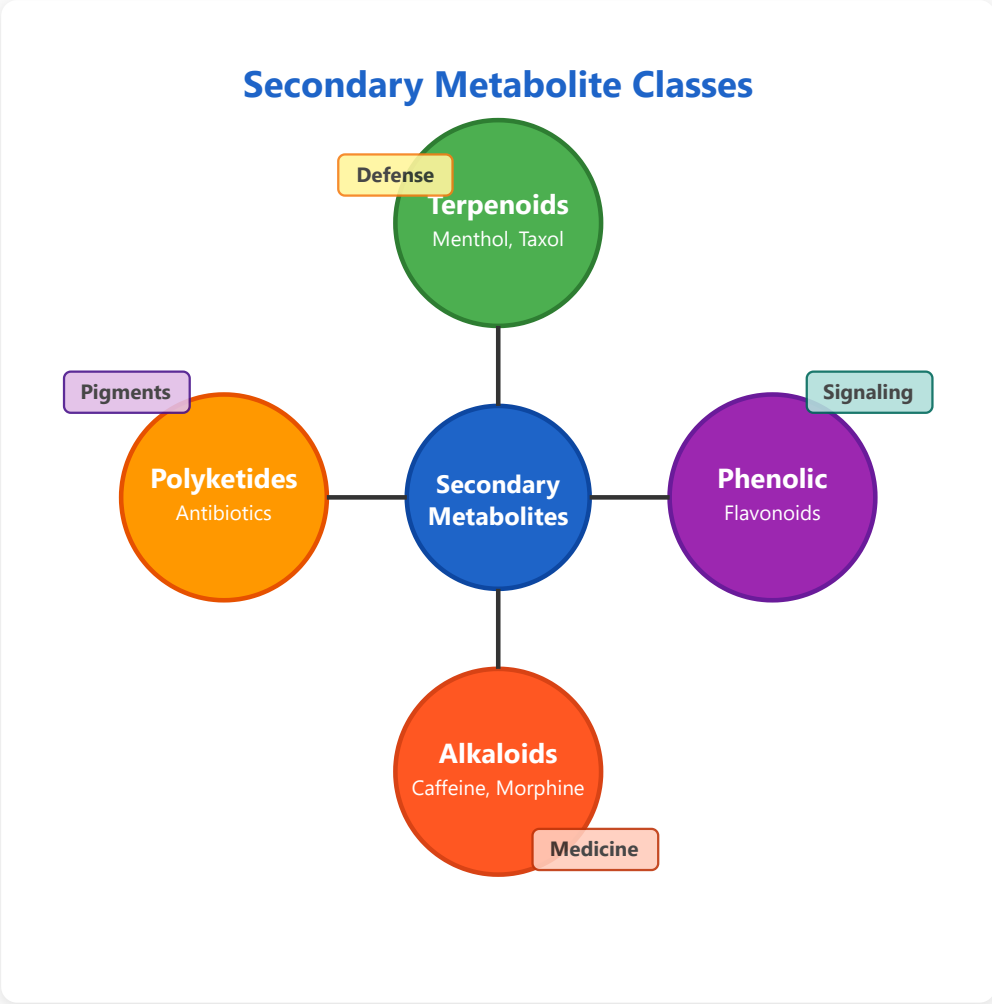
Major Classes

- **Terpenoids:** Diverse structures from isoprene units (e.g., menthol, taxol, steroids)
- **Phenolic Compounds:** Aromatic rings with hydroxyl groups (flavonoids, tannins)
- **Alkaloids:** Nitrogen-containing compounds (caffeine, morphine, nicotine)
- **Polyketides:** Complex structures from acetyl/malonyl-CoA (antibiotics)

Functions

- **Defense:** Toxins against herbivores and pathogens
- **Signaling:** Inter-organism communication
- **Competition:** Allelopathic compounds
- **Attraction:** Pigments and fragrances

Pharmaceutical Importance



Many drugs originate from secondary metabolites: aspirin (salicylic acid), penicillin, taxol (anticancer), artemisinin (antimalarial).

4. Metabolic Flux Analysis

Concept

Metabolic flux measures the rate at which metabolites flow through metabolic pathways, providing dynamic insight beyond static concentration measurements.

Isotope Tracing Methods

- **^{13}C Labeling:** Tracks carbon atom fate through pathways (e.g., [U-^{13}C]glucose)
- **^{15}N Labeling:** Follows nitrogen metabolism in amino acids and nucleotides
- **^{2}H (Deuterium):** Monitors hydrogen exchange and lipid synthesis

Applications

- **Cancer Metabolism:** Identify altered flux in Warburg effect and glutamine addiction
- **Drug Discovery:** Target specific pathway bottlenecks
- **Metabolic Engineering:** Optimize production strains
- **Disease Mechanisms:** Understand metabolic reprogramming

Analytical Workflow

Isotope-labeled substrate → Cell/tissue incubation → Sample extraction → MS/NMR analysis → Computational modeling → Flux calculation