Table 7.1. Some secondary metabolites derived from different pathways and precursors [after Deacon, 2006]

Precursor	Pathway	Metabolites; representative organisms
Sugars		Few, e.g. muscarine (*Amanita muscaria*) kojic acid (*Aspergillus* spp.)
Aromatic amino acids	Shikimic acid	Some lichen acids
Aliphatic amino acids	Various, including peptide synthesis	Penicillins (*P. chrysogenum, P. notatum*) Fusaric acid (*Fusarium* spp.) Ergot alkaloids (*Claviceps, Neotyphodium*) Lysergic acid (*Claviceps purpurea*) Sporidesmin (*Pithomyces chartarum*) Beauvericin (*Beauveria bassiana*) Destruxins (*Metarhizium anisopliae*)
Organic acids	TCA cycle	Rubratoxin (*Penicillium rubrum*) Itaconic acid (*Aspergillus* spp.)
Fatty acids	Lipid metabolism	Polyacetylenes (Basidiomycota fruitbodies and hyphae)
Acetyl-CoA	Polyketide	Patulin (*Penicillium patulum*) Usnic acid (many lichens) Ochratoxins (*Aspergillus ochraceus*) Griseofulvin (*Penicillium griseofulvum*) Aflatoxins (*A. parasiticus, A. flavus*)
Acetyl Co-A	Isoprenoid	Trichothecenes (*Fusarium* spp.) Fusicoccin (*Fusicoccum amygdali*) Several sex hormones: sirenin, trisporic acids, oogoniol, antheridiol Cephalosporins (*Cephalosporium* and related fungi) Viridin (*Trichoderma virens*)

- Examples of secondary metabolites:
  - Penicillin, griseofulvin, other antibiotics
  - Pigments such as melanin and carotenoid
  - Plant hormones like gibberellins
  - Pharmaceuticals like ciclosporin A
  - Aflatoxins
  - Ergot alkaloids
- Why secondary metabolism, especially since they hold no apparent selective advantage (i.e., genes should be lost)?
  - Necessary as escape valve for intermediates of primary metabolic pathways when growth is restricted
  - Provide a selective advantage that is yet to be made obvious
- Key intermediate pathways and precursors include those shown in Table 7.1 of Deacon

- Anaplerotic reactions include:
  - Production of oxaloacetate from pyruvate by the addition of carbon dioxide
  - Glyoxylate pathway - a type of short-circuited TCA pathway
    - Isocitrate is converted to glyoxylate, which is then converted to malate, which then forms oxaloacetate.
    - Oxaloacetate is used to form PEP/sugars

Lysine Biosynthesis

- Lysine is an essential amino acid that is not naturally produced by human and many animals
- Two pathways found in microbes and plants for producing lysine
  - DAP - □-diaminopimleic acid precursor
  - AAA - □-aminoadipic acid precursor
- DAP pathway is used by plants, bacteria, and the Oomycota
- AAA pathway is used by chitin-containing fungi and some euglenids
- Divergence of these pathways is evolutionarily signficant

Secondary Metabolism

- Secondary metabolism refers to a diverse range of metabolic reactions not directly or obviously involved in normal cellular growth
- Thousands of secondary metabolites have been described by fungi
- Common features of secondary metabolites from fungi include:
  - Tend to be produced at the end of exponential growth or during substrate-limited conditions
  - Produced from common metabolic intermediates, but use specialized pathways encoded by specific genes
  - Not essential for growth or normal metabolism
  - Production tends to be genus-, species-, or strain-specific
- Collectively, these commonalities tend to argue for tight regulatory control of secondary metabolism

Biology of Fungi, Lecture 8: Fungal Metabolism and Fungal Products

Energy Acquisition

- Fungi use glycolysis and the tricarboxylic acid (TCA) pathways to
  - Generate energy
  - Provide biosynthetic precursors
- Glycolysis
  - Glucose is converted to pyruvic acid
  - Pyruvic acid is a key intermediate
- Fate of pyruvic acid
  - Oxygen present - transported to the mitochondrion, converted to acetyl-coenzyme A which is then processed through the TCA cycle
  - Oxygen absent/limiting - undergoes fermentation to produce
    - Ethanol (via acetylaldehyde)
    - Lactic acid
- Energy yield
  - Aerobic respiration - 38 potential ATPs produced per glucose molecule; actual yield is lower
    - Use of intermediates for other reactions
    - Use of NADP/NADPH for re-dox reactions
  - Fermentation - 2 ATP molecules
- Use of alternative terminal electron acceptors
  - Some fungi use nitrate instead of oxygen as terminal electron acceptor
    - Yields potentially 26 ATPs per glucose
    - Lower due to differences in ATP generation in the electron transport chain
  - Considered anaerobic respiration (as opposed to aerobic respiration when oxygen is used)

Balancing the Pathways

- Intermediates of glycolysis and the TCA pathway are used to make other substances
- How does the cell replace these components to maintain energy production?

Answer: **Anaplerotic reactions**