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

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

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 redox 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