Folate ("One-Carbon") Pathways

Click on any blue box to see details
(Start with the section with ‘Diet’ and follow the paths with red arrows)

Diet:
- THF
- DHF
- Folate

- Connects to Amino Acids
- Donates one carbon (from Ser, Gly)

- THF
- DHF
- Folate

- Connects to Nucleic Acids
- Lectures

- Methyl-THF
- Methylene-THF
- Formyl-THF

- THF Cycle
- Methionine Cycle

- Purine biosynthesis
- Thymidylate synthetase
Folic Acid is Synthesized By Bacteria

Dietary folate: folic acid (meats, green veggies)
*requires* the intestinal enzyme ‘Conjugase’ for absorption.
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
The diagram illustrates pathways involving folate metabolism, including:

- **Biosynthesis of methionine** from N4-methyl tetrahydrofolate.
- **Biosynthesis of thymidylate** from N4, N6-methylene tetrahydrofolate.
- **Biosynthesis of purines** from N4-formyl tetrahydrofolate.

The diagram also shows the interaction with glycine (Gly) and serine (Ser) in the pathway.
Methionine Cycle
And Biological Methyl Groups

Methionine

S-Adenosyl Methionine

S-Adenosyl Homocysteine

Homocysteine

Serine

Cysteine

(remainder of homocysteine degraded for energy)
N\textsuperscript{6} -methyl THF

homocysteine

vitamin B\textsubscript{12}

methionine
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

\[ \text{N}^\circ, \text{N}^\circ \text{ methylene tetrahydrofolate} \]

methionine

\[ \text{N}^\circ \text{ methyl tetrahydrofolate} \]

homocysteine

\[ \text{NAD}^+ + \text{H}^+ \]
Other methyl acceptors:

DNA ("CpG Islands")
RNA
Folate Deficiencies: Symptom: megaloblastic anemia

Dietary deficiency:
Common especially in developing countries, lower socioeconomic classes
Folate deficiency secondary to bowel irritation:

- Conjugase is essential for adequate absorption of dietary folates

- Conjugase production may be compromised by bowel irritation:
  
  ‘Tropical Sprue’ - bowel irritation probably arising from bacterial origin, causes intestinal inflammation and malabsorption.

  ‘Celiac Sprue’ - similar outcome, but the original irritation is due to an allergic response, for example to gliaden (a component in gluten)
Folate Deficiency Secondary to B12 deficiency: the ‘methyl trap’ hypothesis

B12 is also critical in other reactions, ones for which the deficiency has serious neurological consequences.