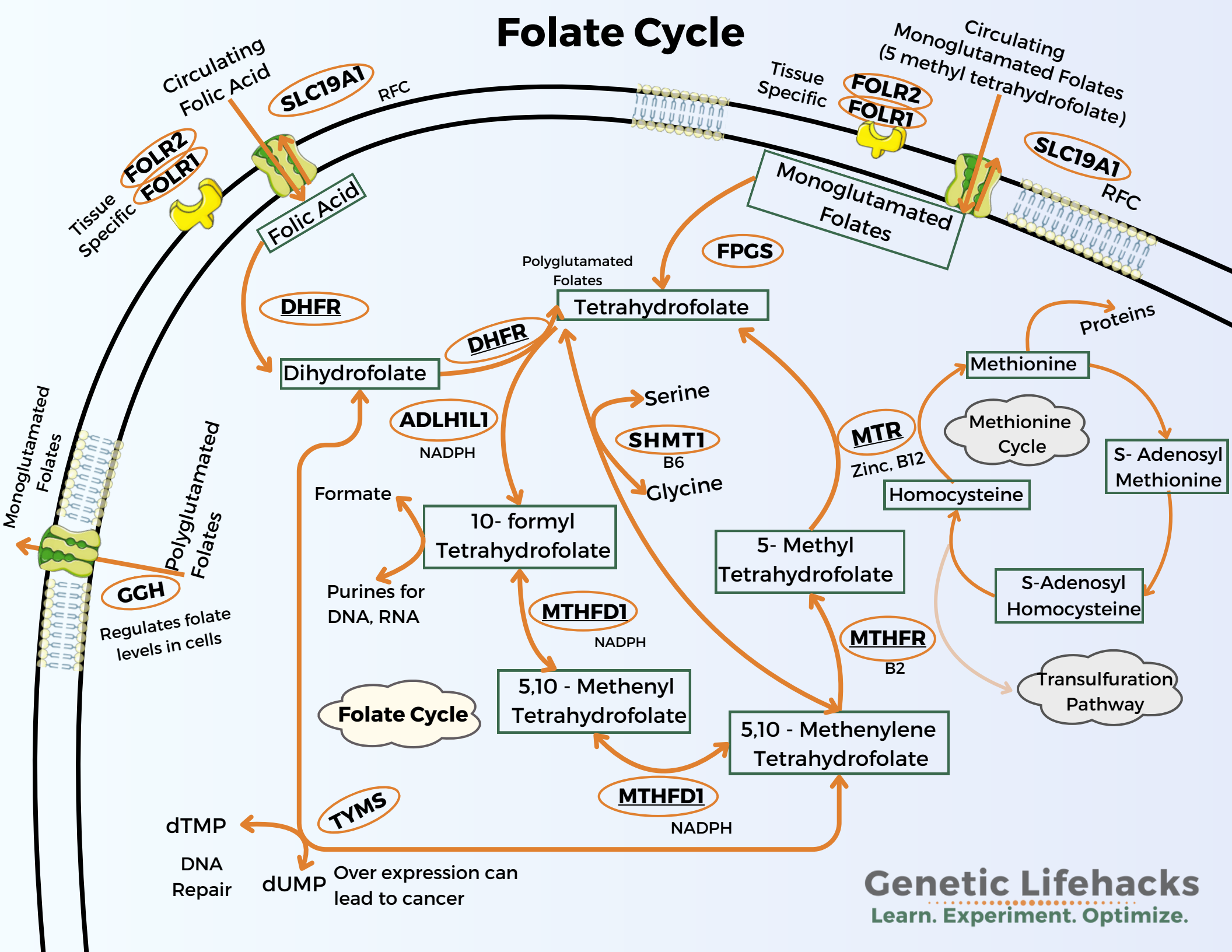
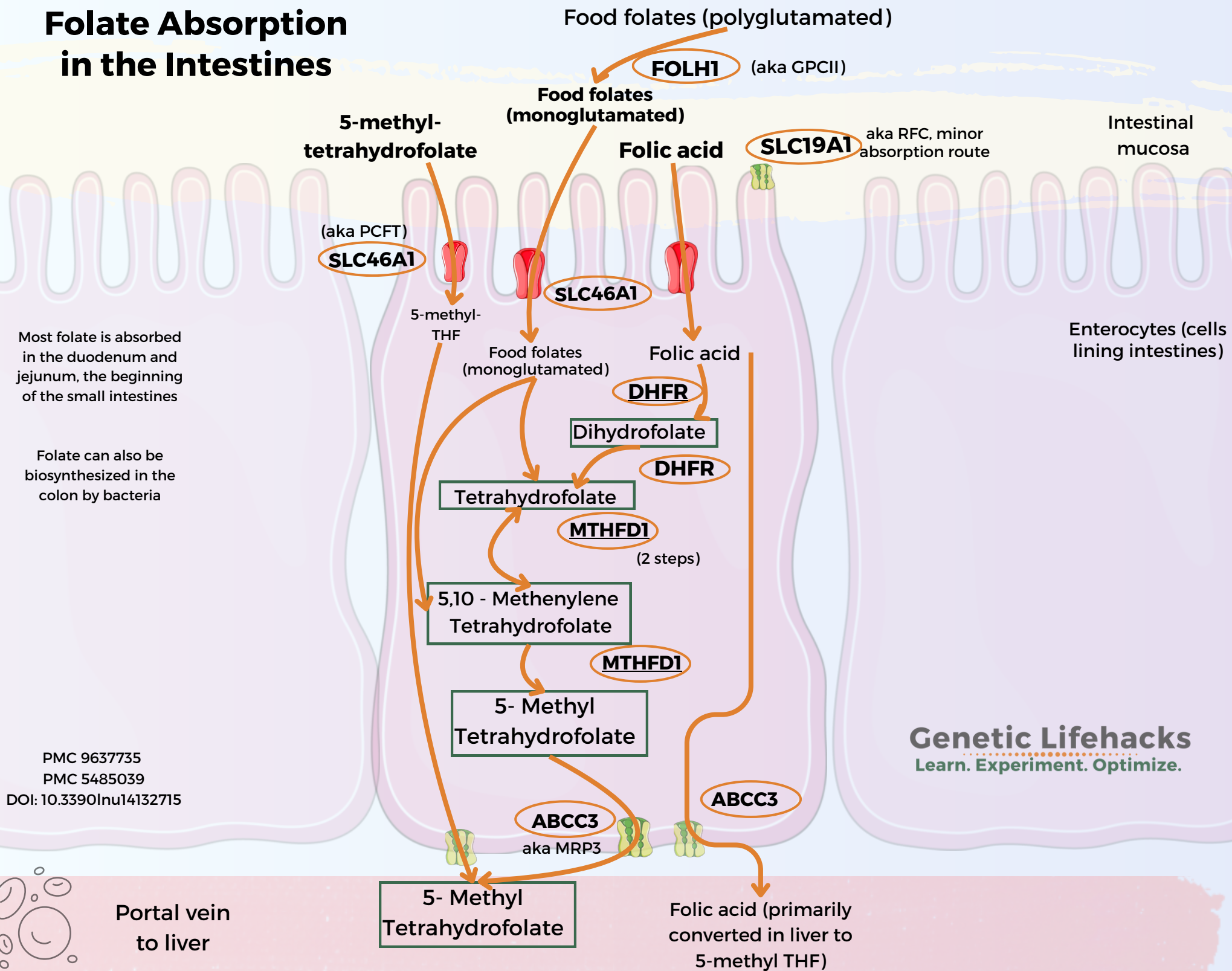


Folate Cycle



Folate Absorption in the Intestines



Most folate is absorbed in the duodenum and jejunum, the beginning of the small intestines

Folate can also be biosynthesized in the colon by bacteria

PMC 9637735
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Folate Cycle Genes

SLC19A1

- Reduced folate carrier, RFC1
- Receptor
- Transports folic acid, 5-methyltetrahydrofolate into cells
- Transports thiamine and other anions, out of cells
- Widely expressed in all tissue

FOLR1

- Folate receptor alpha
- Receptor
- Moves folate into cells, endocytosis
- Involved in folate in the brain
- Also found in kidneys, ovary, fallopian tubes

FOLR2

- Folate receptor beta
- Receptor
- Moves folate into cells, endocytosis
- Found in macrophages, placenta, adipose tissue

SLC46A1

- Proton-coupled folate receptor, PFCT
- Receptor
- Intestinal absorption of monoglutamated folates
- Found in small intestines, liver, brain barrier

FOLH1

- Folate hydrolase 1, PSMA
- Enzyme that converts polyglutamated folates from food into monoglutamated folates that can be absorbed via SLC46A1
- Expressed in intestinal mucosa, prostate

DHFR

- Dihydrofolate reductase
- Enzyme that converts folic acid to dihydrofolate and converts dihydrofolate to tetrahydrofolate
- Widely expressed in cells throughout the body

FPGS

- Folypolyglutamate Synthase
- Enzyme that catalyzes reactions adding glutamates to monoglutamated folates after they are transported into cells
- Widely expressed in cells throughout the body

ADLH1L1

- Aldehyde dehydrogenase 1 family L1
- Enzyme that converts 10-formyl tetrahydrofolate to tetrahydrofolate
- Widely expressed in cells throughout the body

Folate Cycle Genes

MTHFD1

- Methylene tetrahydrofolate dehydrogenase
- Three enzymatic functions within folate cycle
- Widely expressed in cells throughout the body

MTHFR

- Methylene tetrahydrofolate reductase
- Enzyme that converts 5,10 - methylene tetrahydrofolate, a substrate for homocysteine remethylation
- Widely expressed in cells throughout the body

MTR

- 5-methyl tetrahydrofolate - homocysteine methyltransferase
- Enzyme, B12 dependant
- Final step in methionine synthesis

GGH

- Gamma-glutamyl hydrolase
- Enzyme that converts polyglutamated folates to monoglutamated folates for excretion from cells to balance folate levels
- Widely expressed

SHMT1

- Serine hydroxymethyltransferase
- Converts serine to glycine while also converting tetrahydrofolate to 5,10-tetrahydrofolate
- Widely expressed

TYMS

- Thymidylate synthase
- Enzyme that converts deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (dTMP)
- Widely expressed

Folate Cycle Notes and References

Types of supplemental folate:

- Methylfolate, 5-methyltetrahydrofolate
- Folic acid (needs conversion by DHFR)
- Folinic acid (leucovorin, Rx)

Folate absorption:

- Primarily occurs in the duodenum and jejunum
- Bacteria can produce folate in the colon
- Food folates are polyglutamated and must be transformed (FOLH1 gene) for absorption via the proton-coupled folate receptor (SLC46A1)
- Folic acid, methylfolate are monoglutamated and don't need transformation to be absorbed
- SLC46A1 is primary route, reduced folate carrier (SLC19A1) is a minor route
- The pH in the small intestine can influence absorption

Cellular folate:

- The reduced folate carrier (SLC19A1 gene) is a bidirectional transporter and moves anions, such as thiamine metabolites, out of the cell while moving folate in
- Monoglutamated folates (folic acid, methylfolate) are converted in cells to polyglutamated forms to form a folate pool that stays in the cell
- Separate folate pool within mitochondria

Methylation and Methyl Groups:

- CH₃ (carbon + 3 hydrogens)
- Also called a one-carbon unit
- Methyl donors donate a methyl group in reactions (e.g. SAMe, methylB12, TMG)
- Not all compounds containing methyl groups are methyl donors

Genetic Lifehacks Articles (genotype, refs):

[MTHFR](#)

[DHFR](#)

[FOLR1 & FOLR2](#)

[MTR, MTRR](#)

[MTHFD1](#)

References:

PMC3982215

Human Protein Atlas

PMC2728423

PMC5485039

PMC4185403

PMC9637735

PMC5485039

PMC9794768