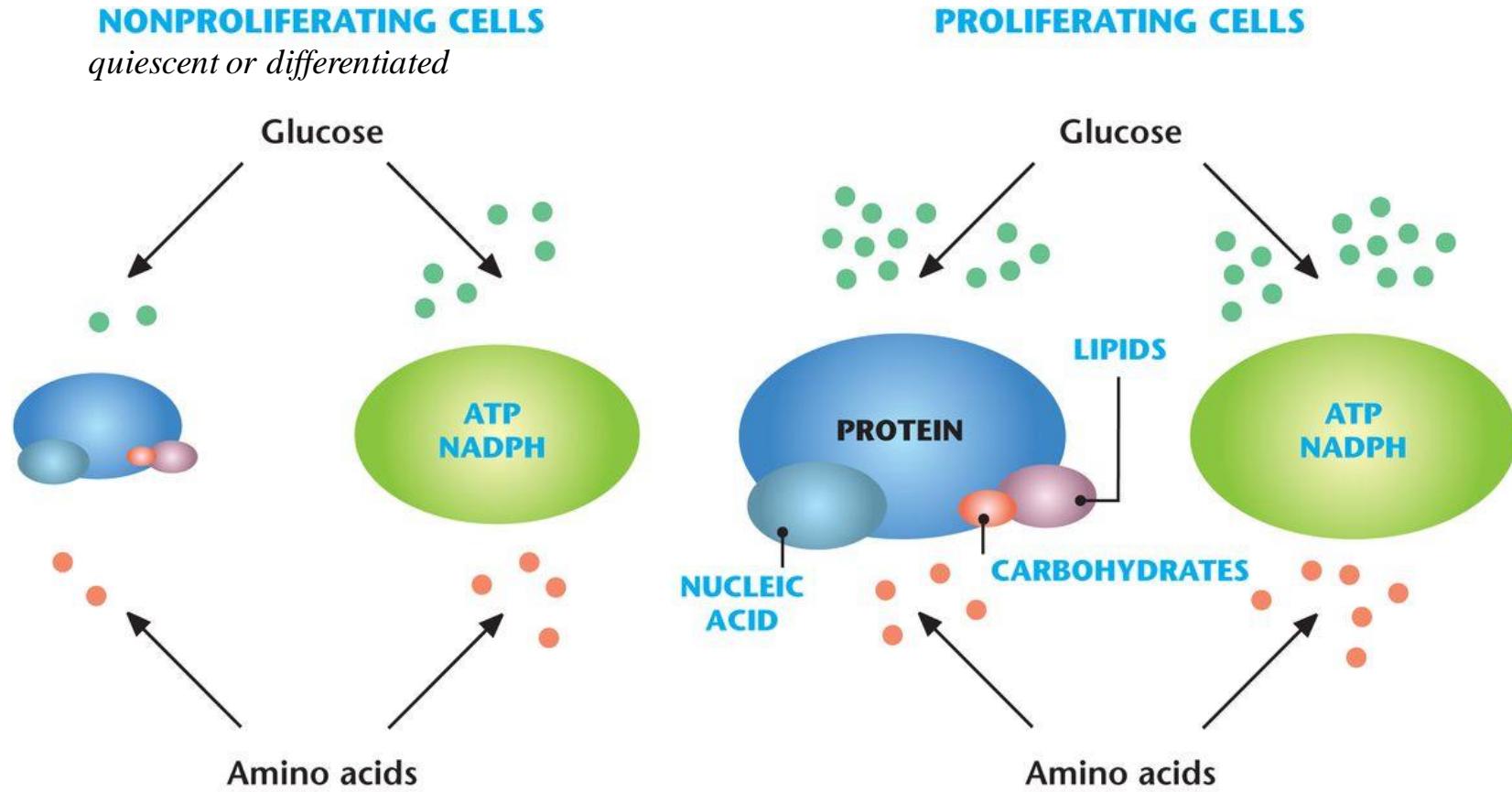


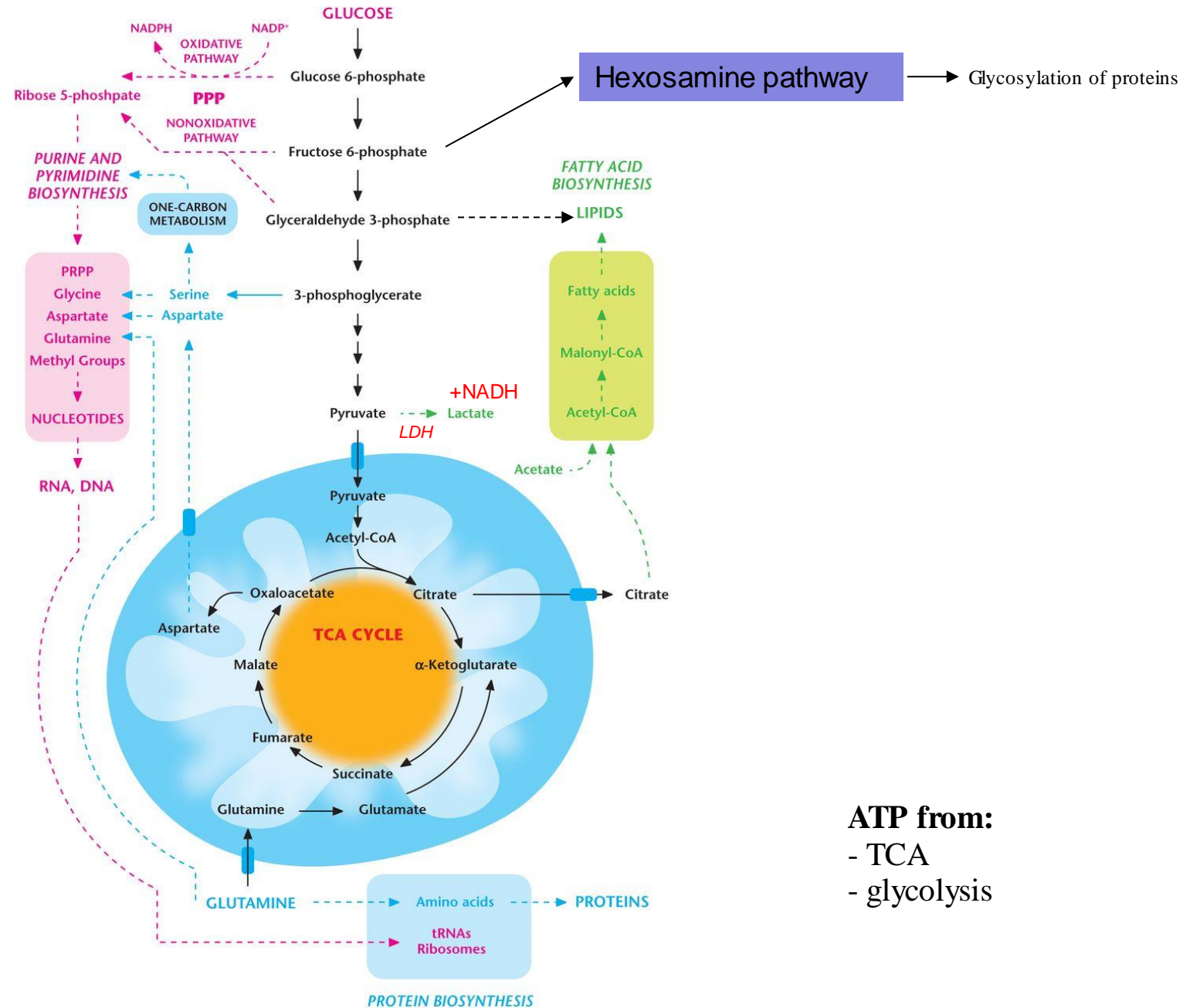
Proliferating versus nonproliferating cells have different metabolic needs.



Housekeeping functions

Housekeeping functions + anabolic reaction + antioxidant functions

Proliferating cells require glycolysis (aerobic glycolysis) and mitochondrial metabolism



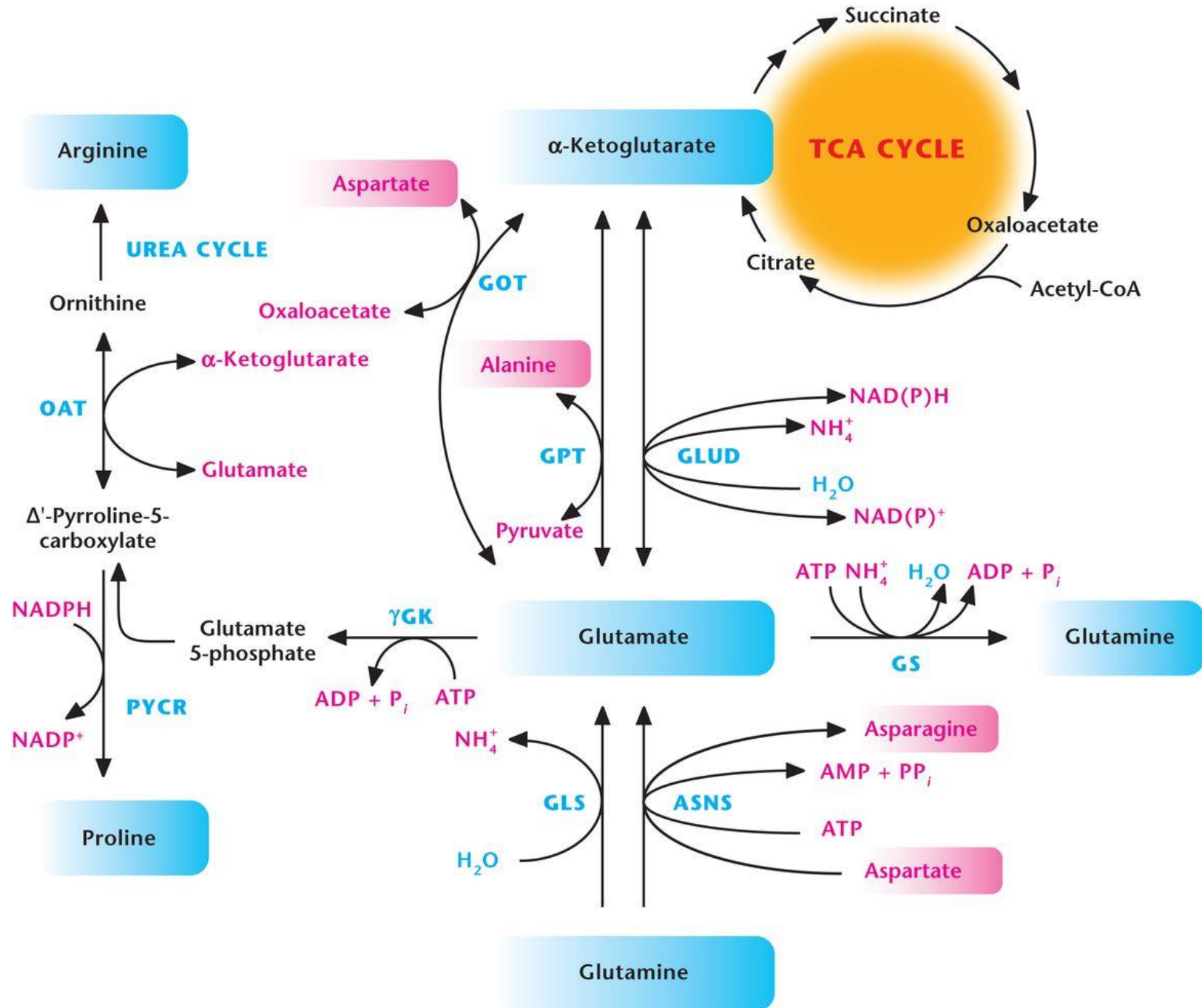
NADPH from:

- PPP
- One carbon metabolism
- IDH
- Malic enzyme

ATP from:

- TCA
- glycolysis

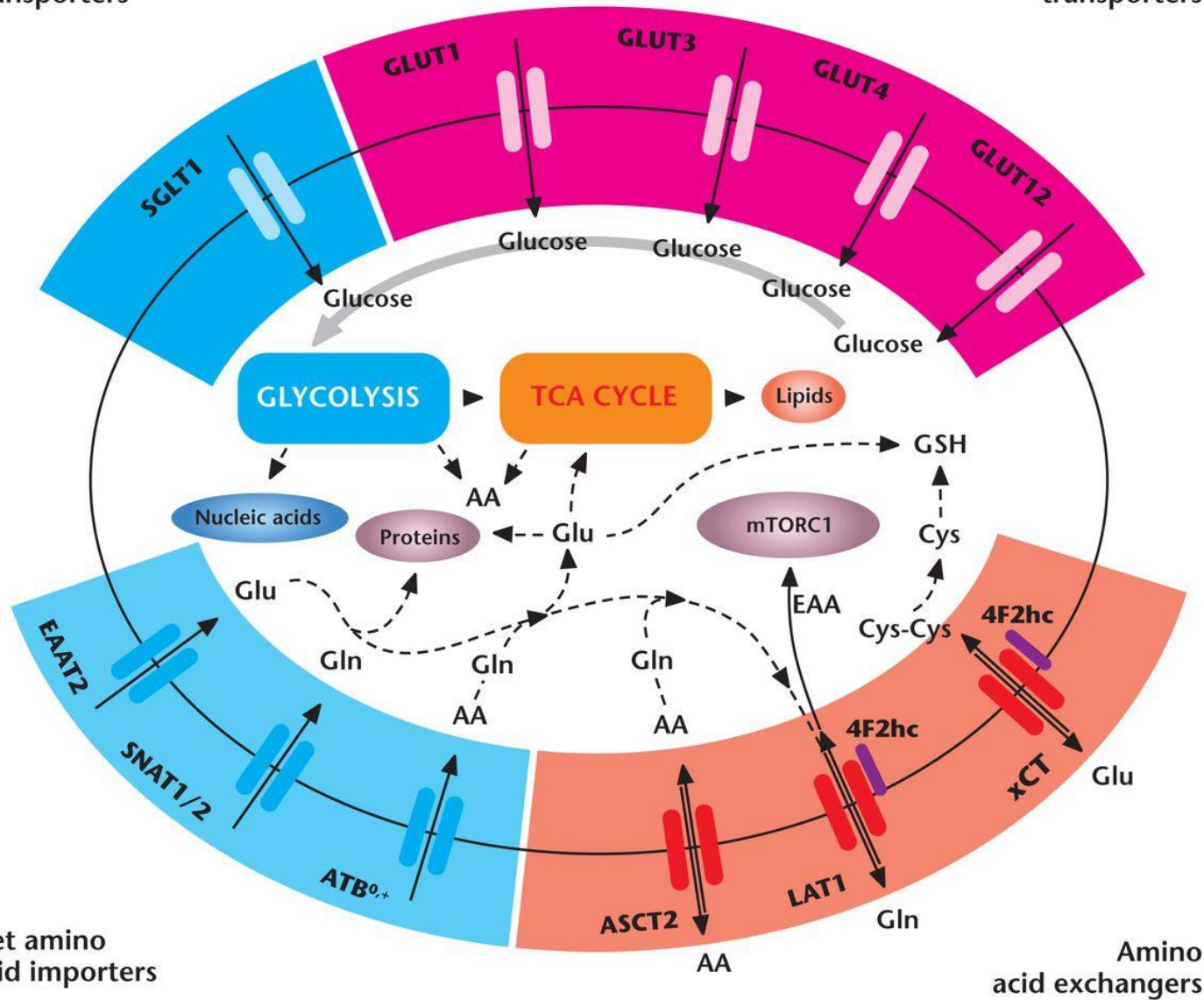
Glutamate generates multiple amino acids.



Cell proliferation requires nutrient transporters

Active glucose transporters

Facultative glucose transporters



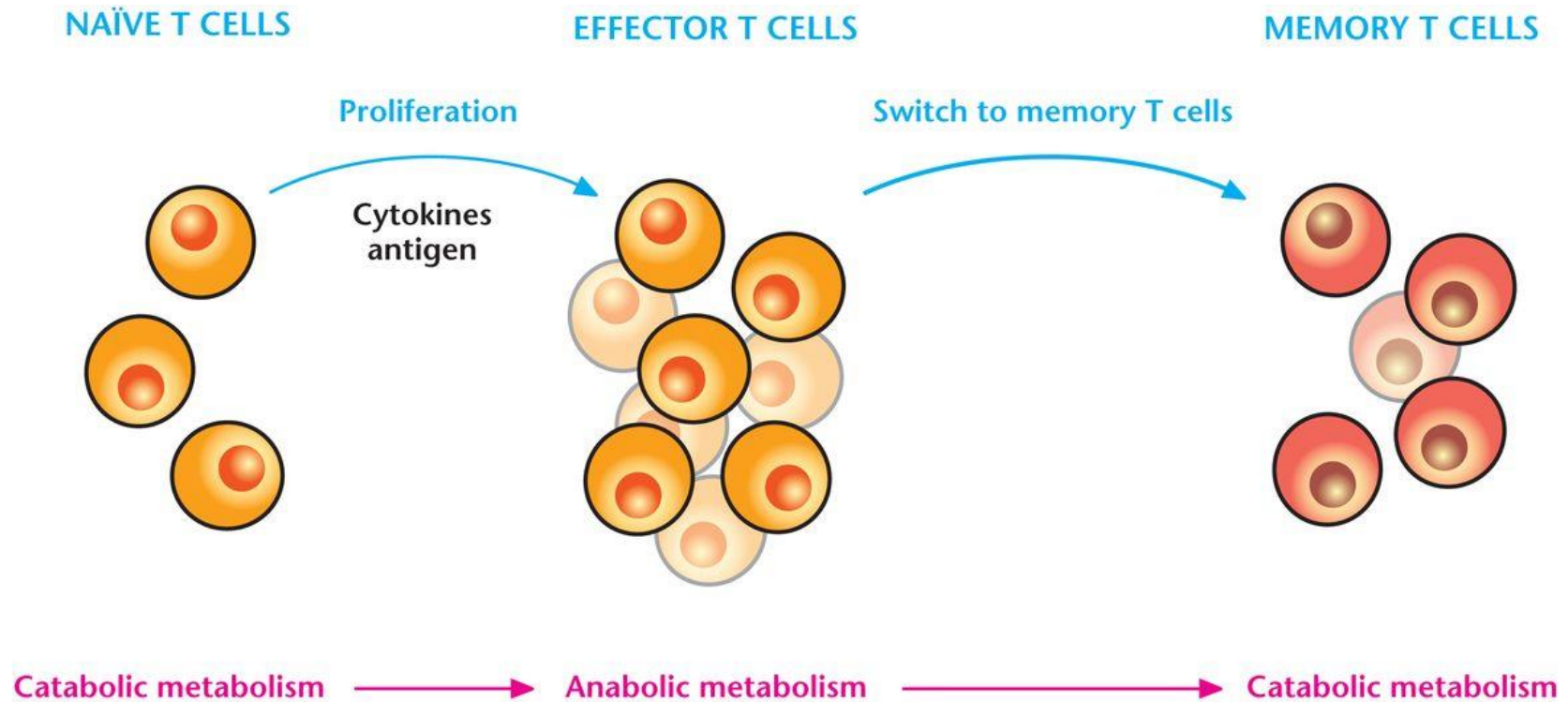
Net amino acid importers

Amino acid exchangers

GLUTs: Glucose transporters

Name	Distribution	Notes
GLUT1	Is widely distributed in fetal tissues. In the adult, it is expressed at highest levels in erythrocytes and also in the endothelial cells of barrier tissues such as the blood–brain barrier. However, it is responsible for the low level of basal glucose uptake required to sustain respiration in all cells.	Levels in cell membranes are increased by reduced glucose levels and decreased by increased glucose levels. GLUT1 expression is upregulated in many tumors.
GLUT2	Is a bidirectional transporter, allowing glucose to flow in 2 directions. Is expressed by renal tubular cells, liver cells and pancreatic beta cells. It is also present in the basolateral membrane of the small intestine epithelium. Bidirectionality is required in liver cells to uptake glucose for glycolysis and glycogenesis, and release of glucose during gluconeogenesis. In pancreatic beta cells, free flowing glucose is required so that the intracellular environment of these cells can accurately gauge the serum glucose levels. All three monosaccharides (glucose, galactose, and fructose) are transported from the intestinal mucosal cell into the portal circulation by GLUT2.	Is a high-frequency and low-affinity isoform. ^[12]
GLUT3	Expressed mostly in neurons (where it is believed to be the main glucose transporter isoform), and in the placenta.	Is a high-affinity isoform, allowing it to transport even in times of low glucose concentrations.
GLUT4	Expressed in adipose tissues and striated muscle (skeletal muscle and cardiac muscle).	Is the insulin-regulated glucose transporter. Responsible for insulin-regulated glucose storage.
GLUT14	Expressed in testes	similarity to GLUT3 ^[12]

T cells engage in different types of metabolism depending on their functions

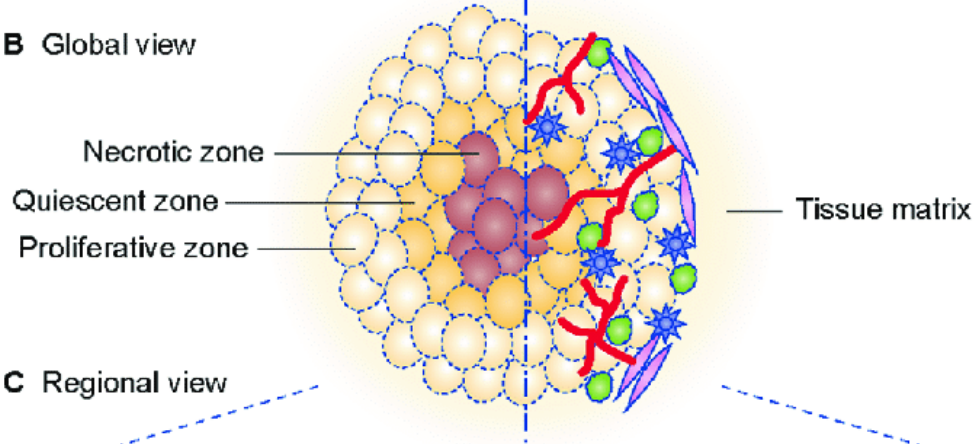


Cancer metabolism heterogeneity

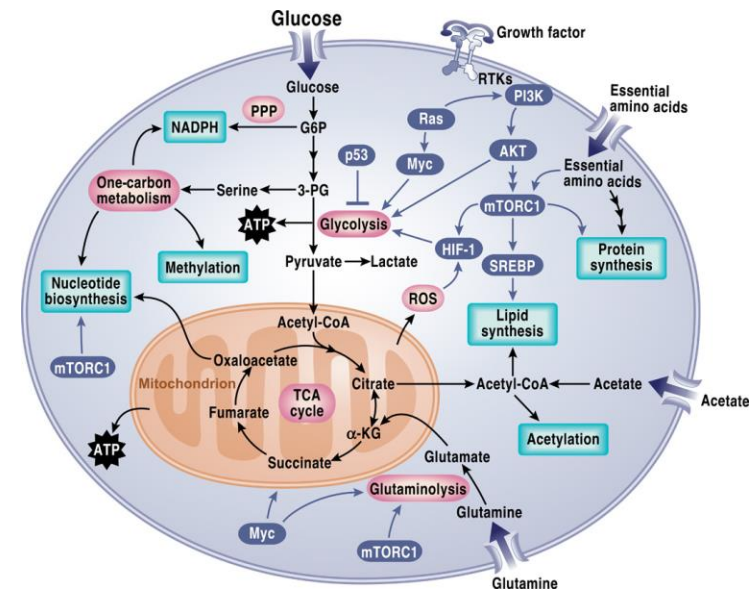
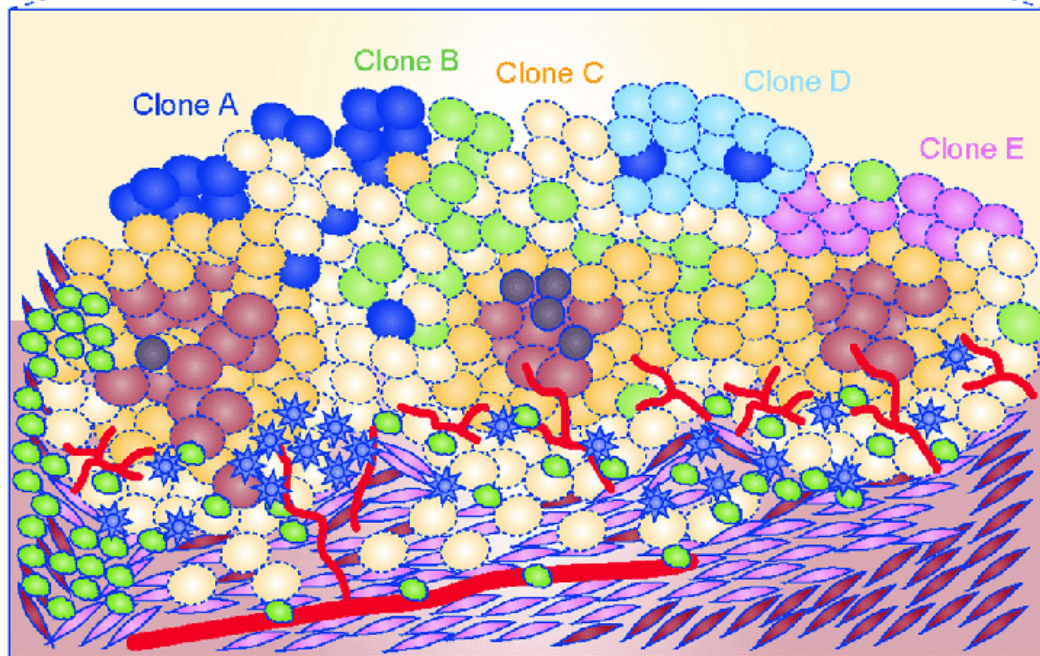
A Gradients



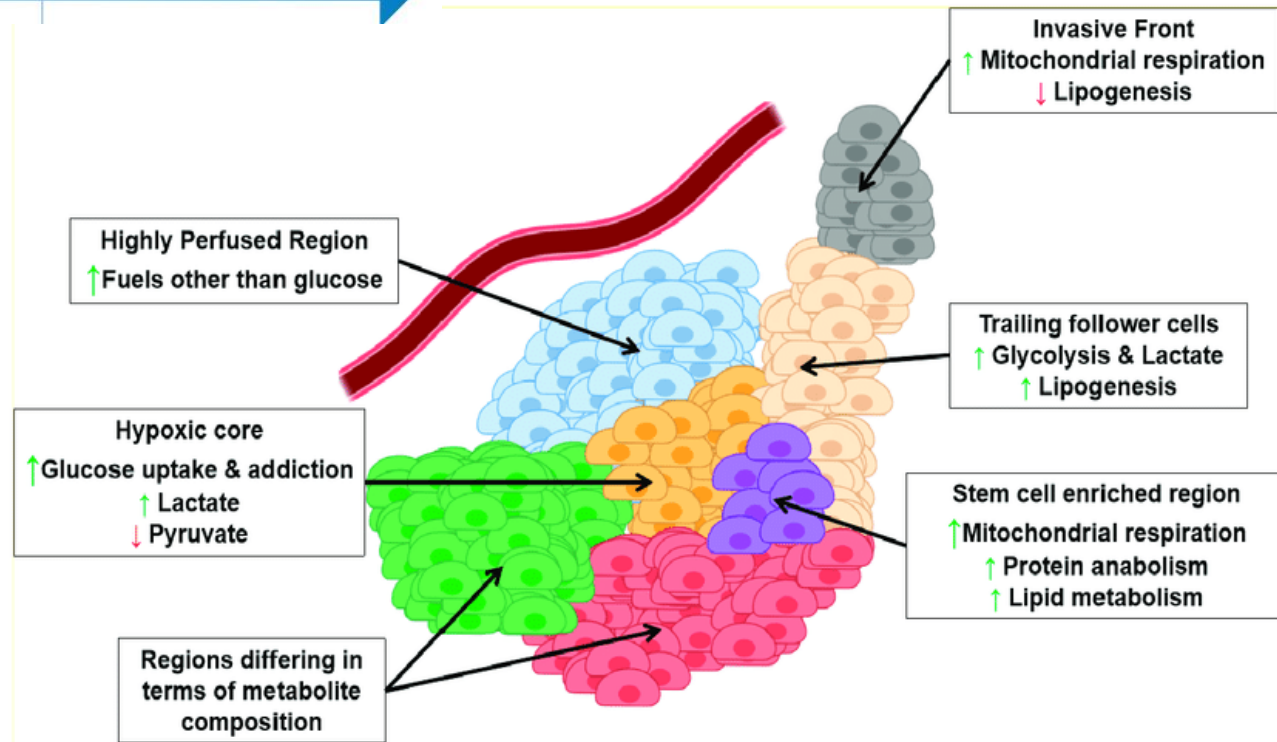
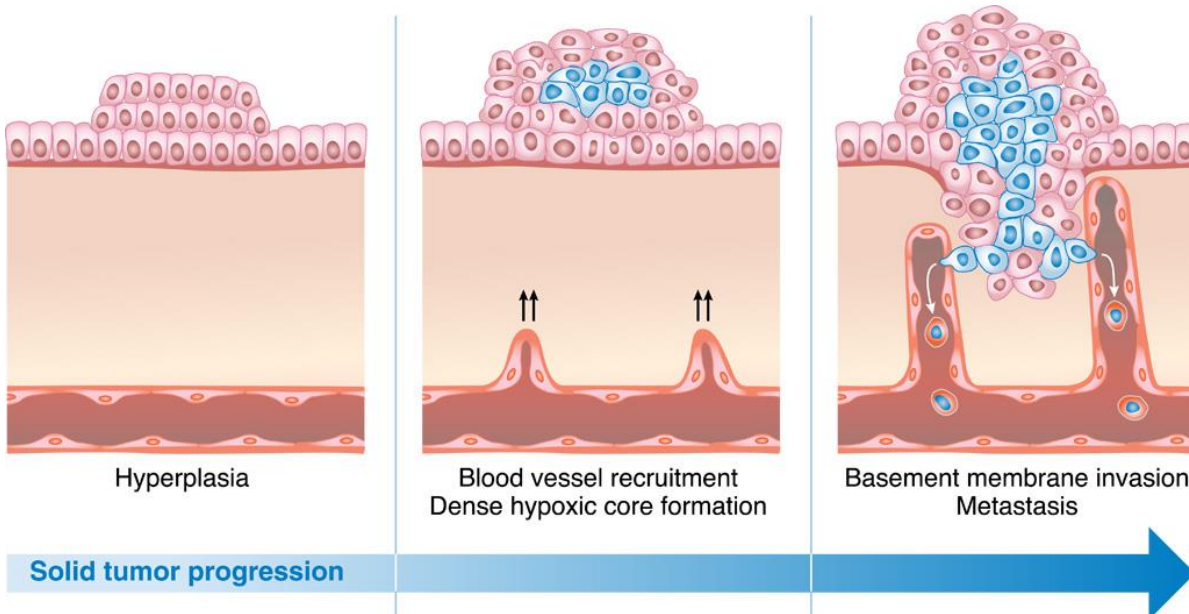
B Global view



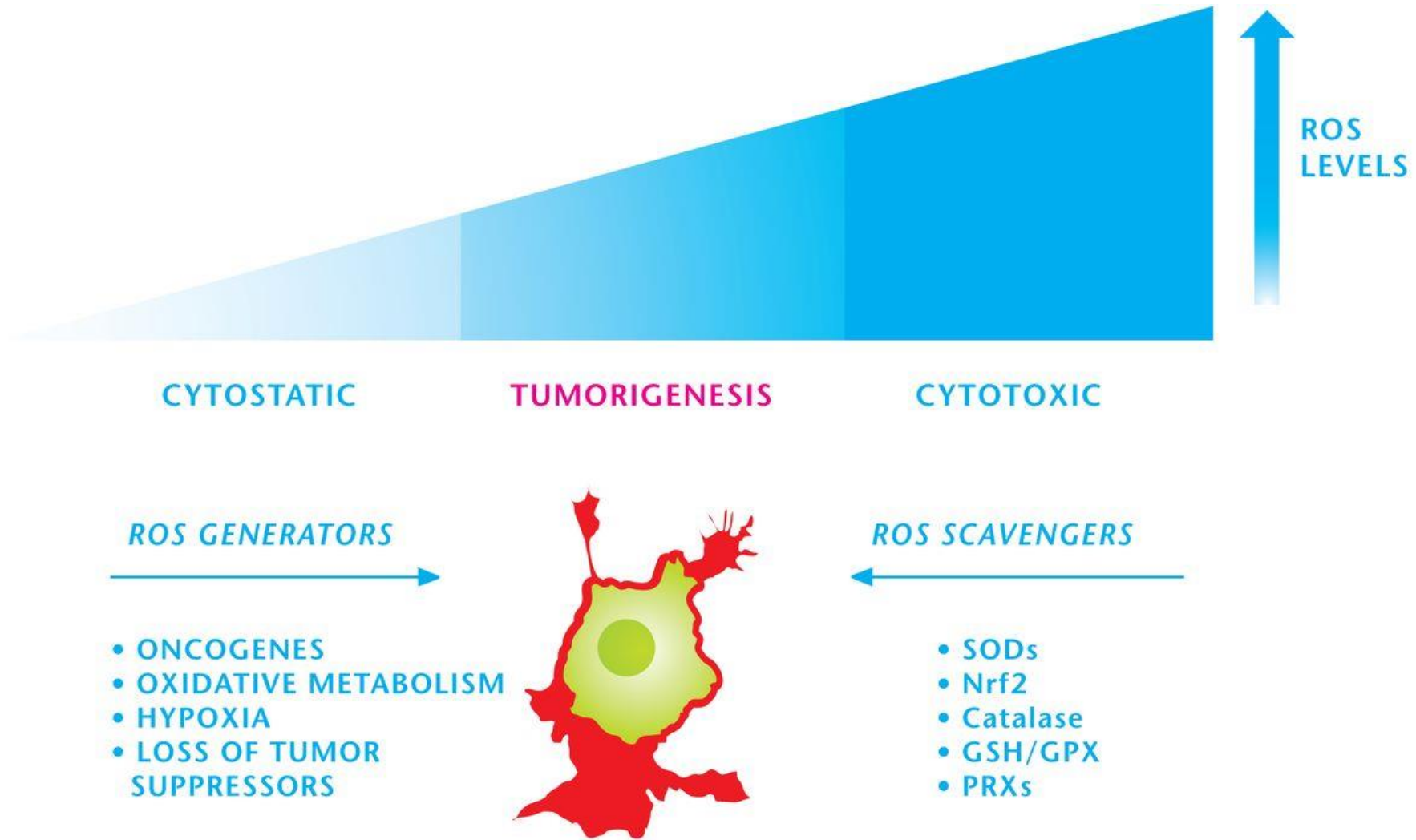
C Regional view



Other example cancer metabolism

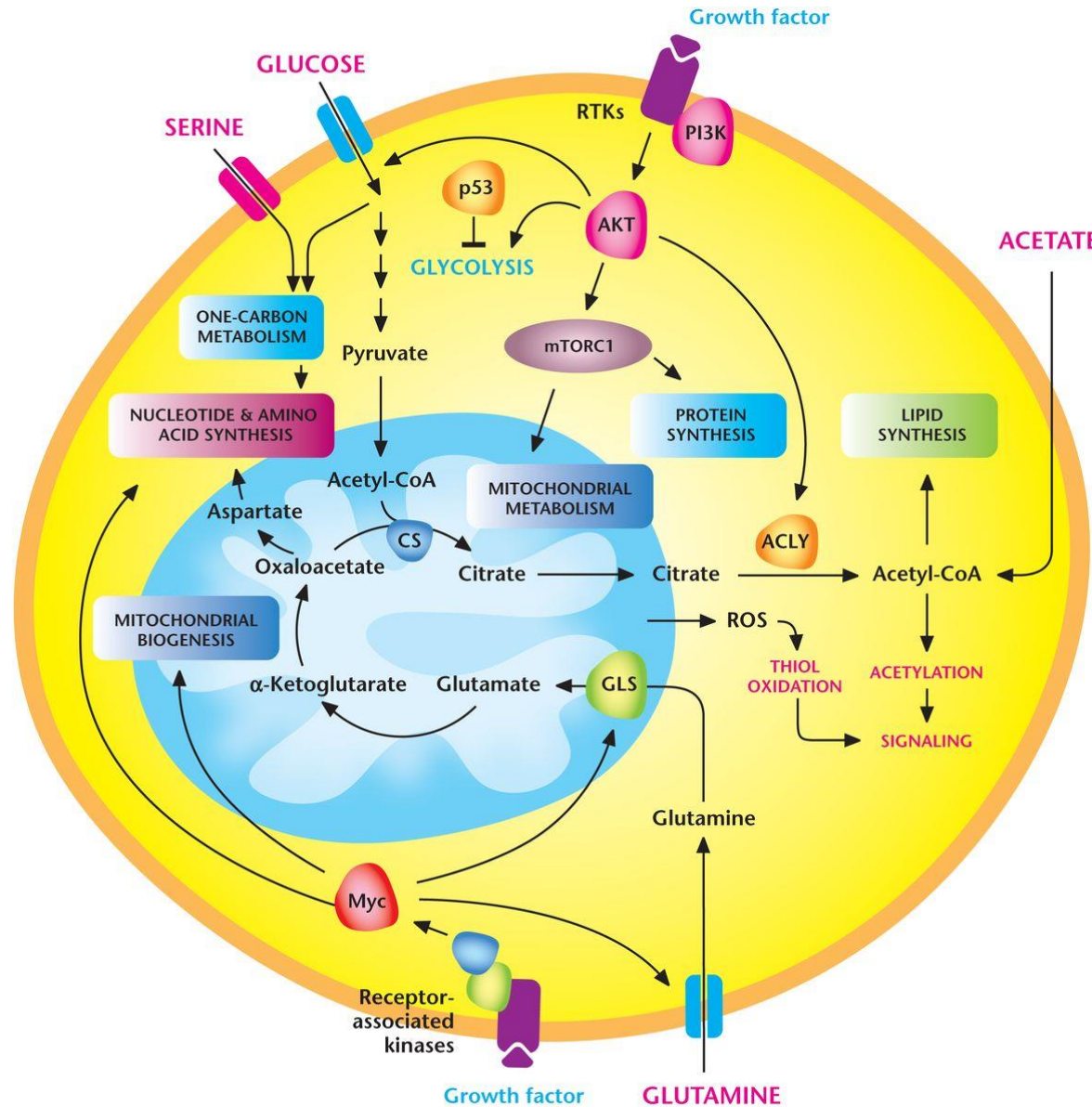


Cancer cells maintain redox balance

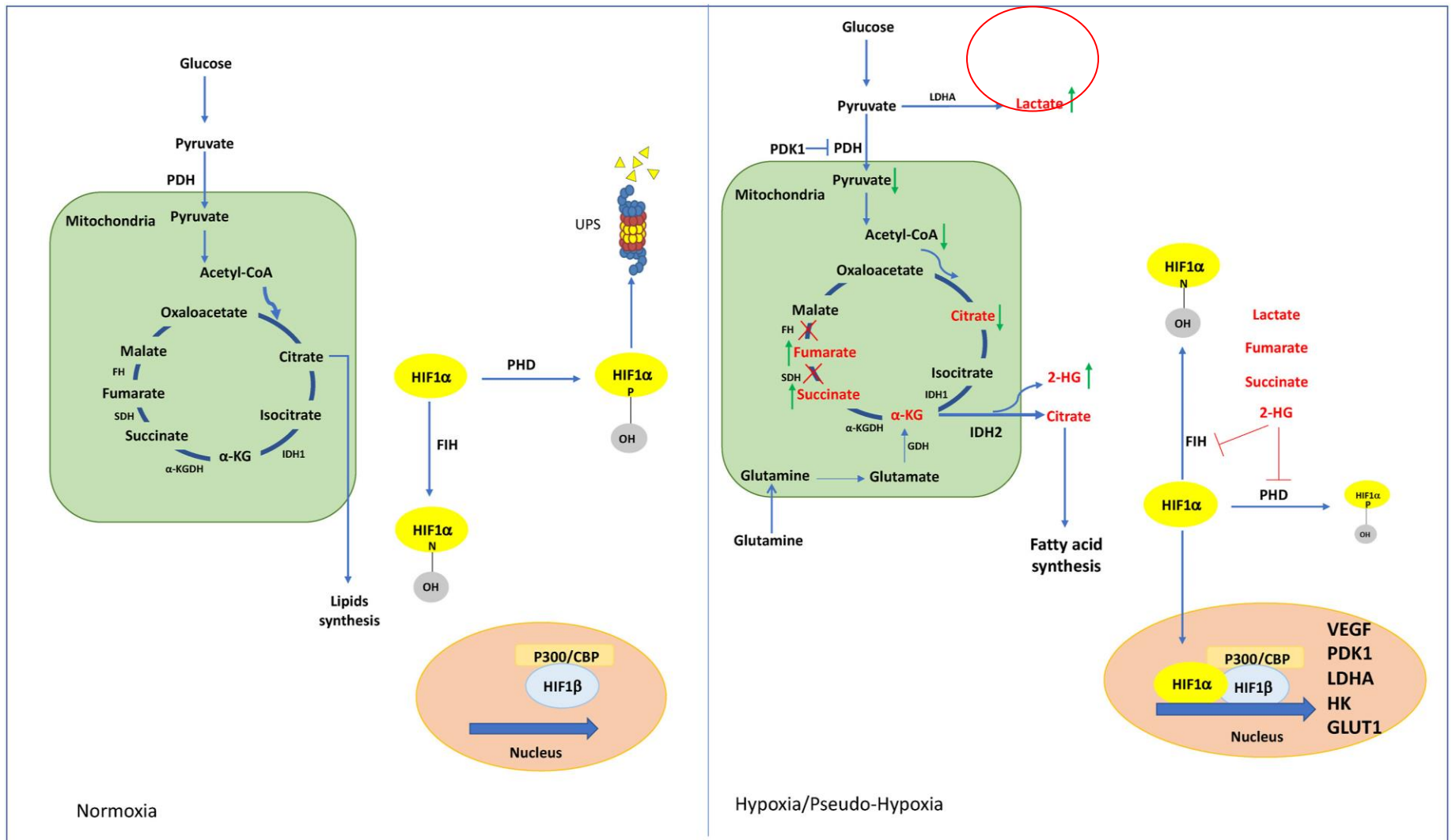
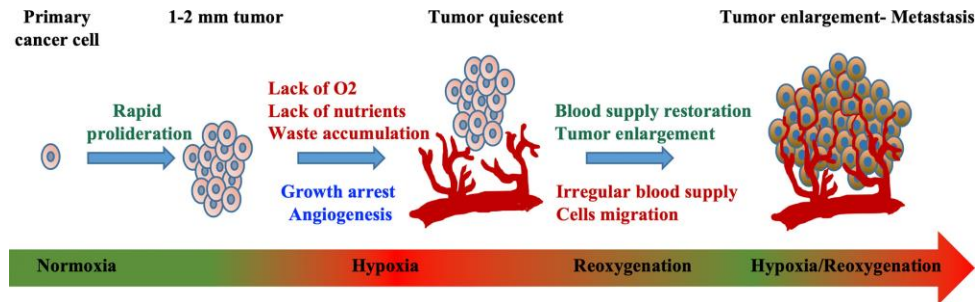


Signaling pathways that regulate cancer cell metabolism

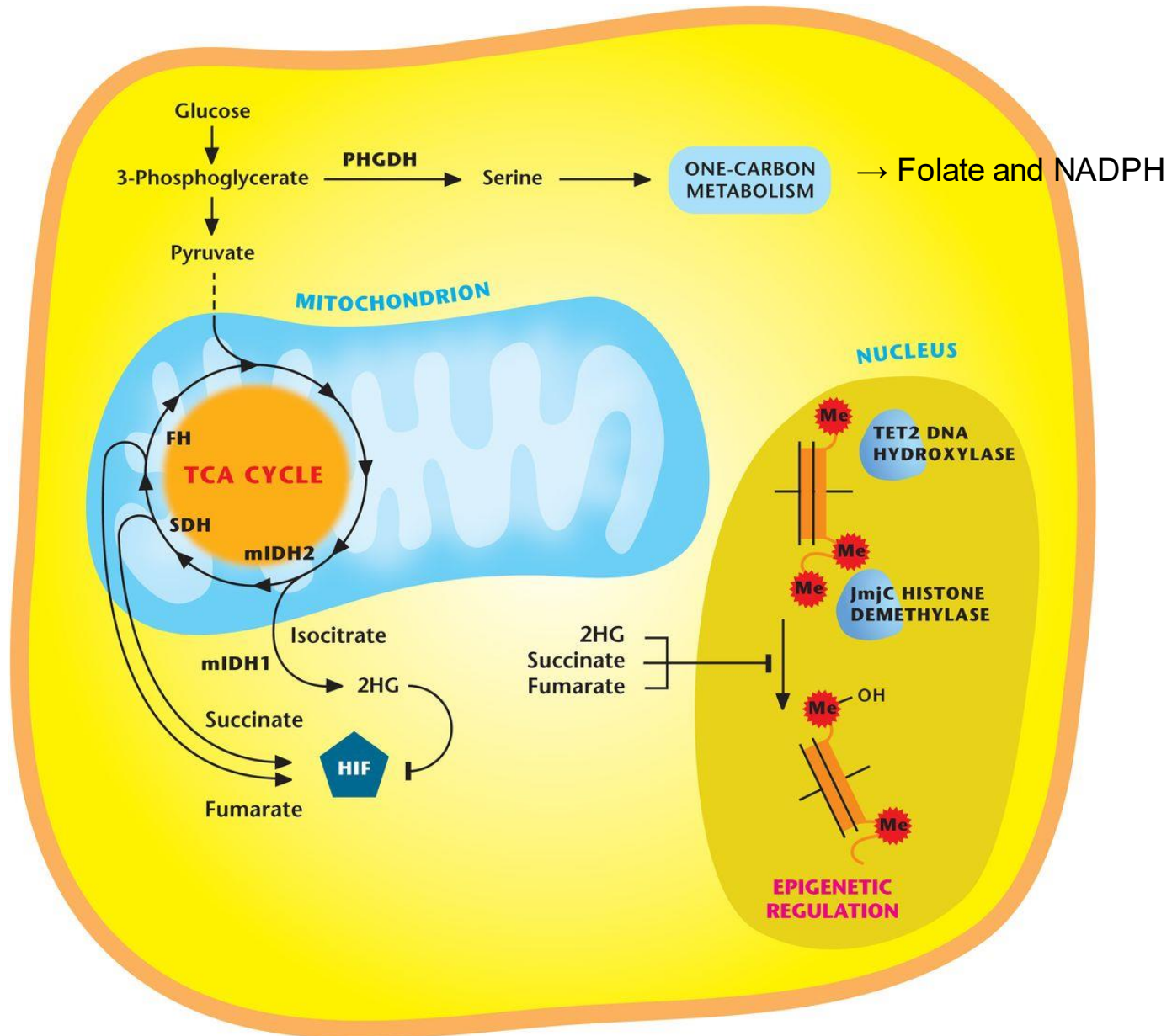
mTOR
Kras
Myc



Metabolic adaptation in hypoxia

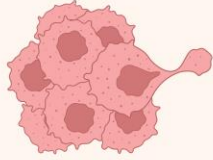


Alterations in certain metabolic enzymes drive cancer

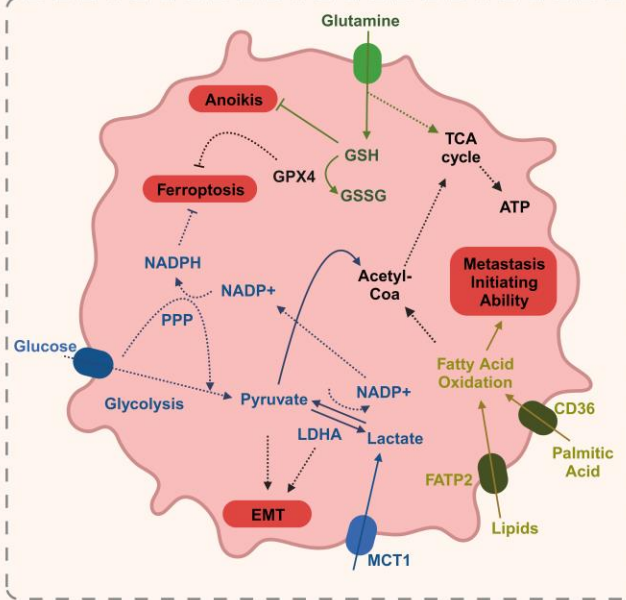


Metabolism and cancer spreading

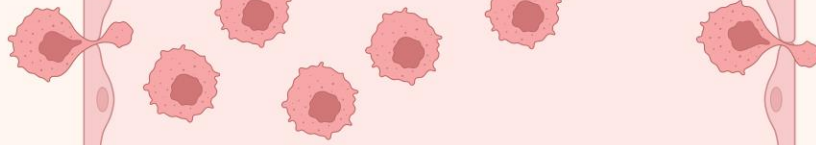
Primary Tumour



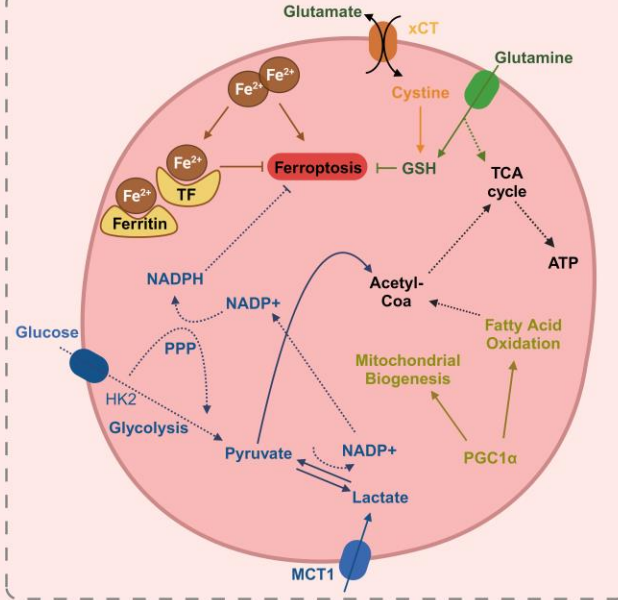
a CTC Formation



CTCs



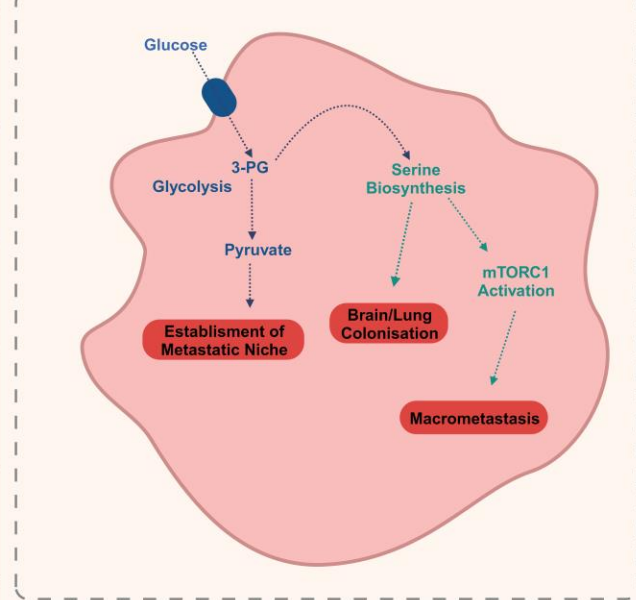
b Survival in Circulation



Secondary Tumour



c Extravasation and Colonisation



Metabolism can be targeted for cancer therapy

Repurposing the antidiabetic drug metformin to reduces tumorigenesis through multiple mechanisms

