

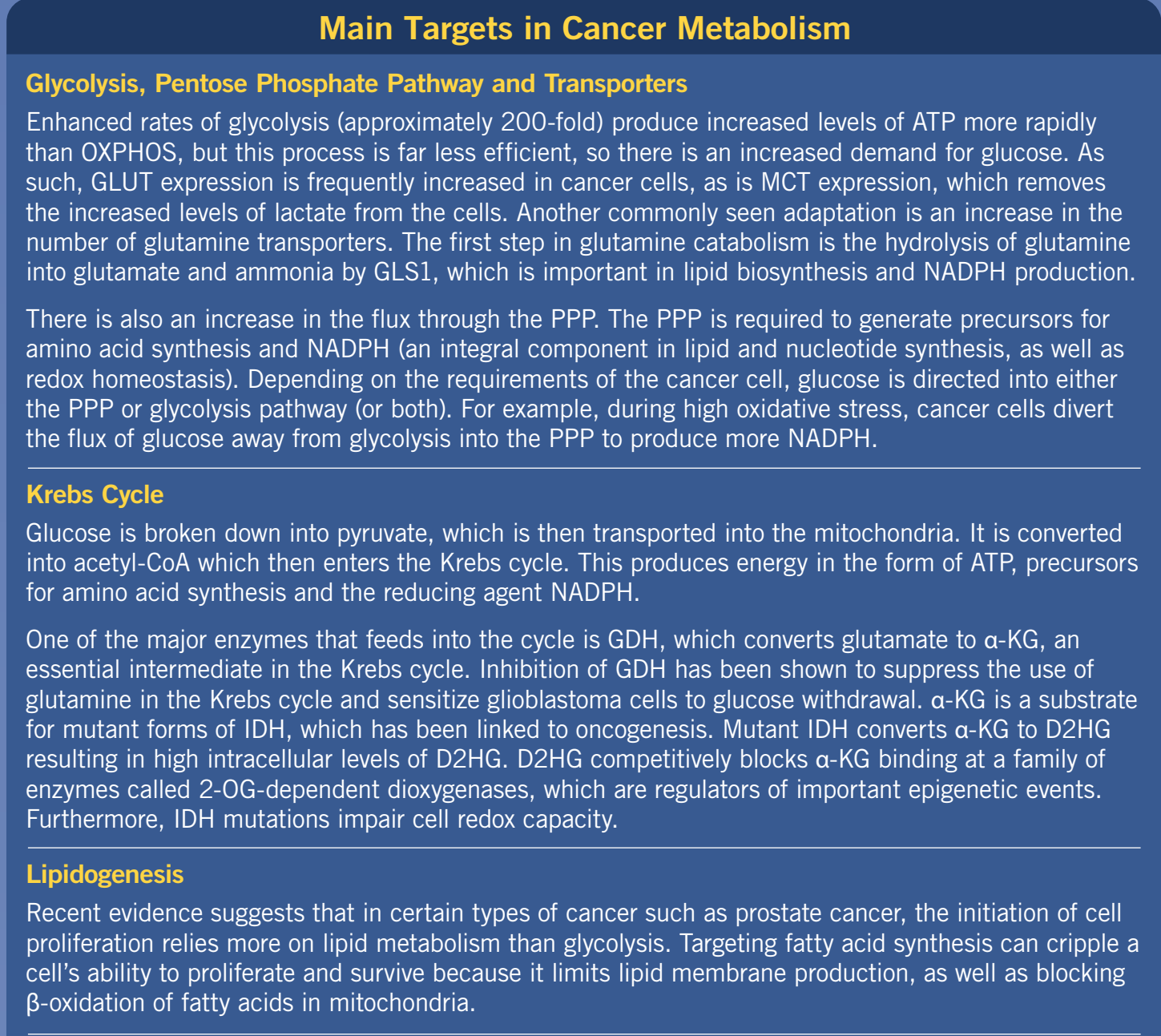
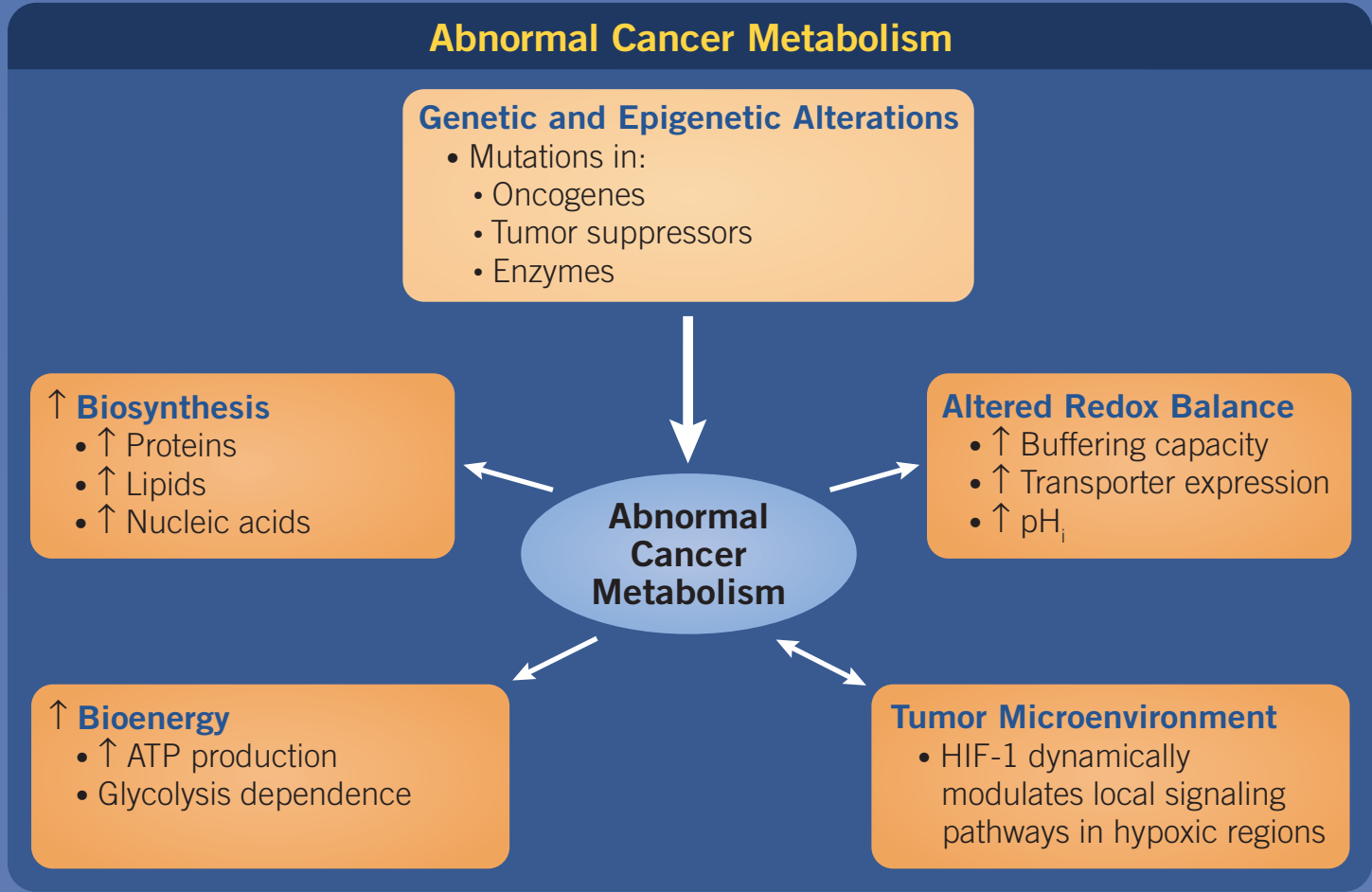
# Cancer Metabolism

Adapted from Edition 3 of the Tocris Cancer Product Guide  
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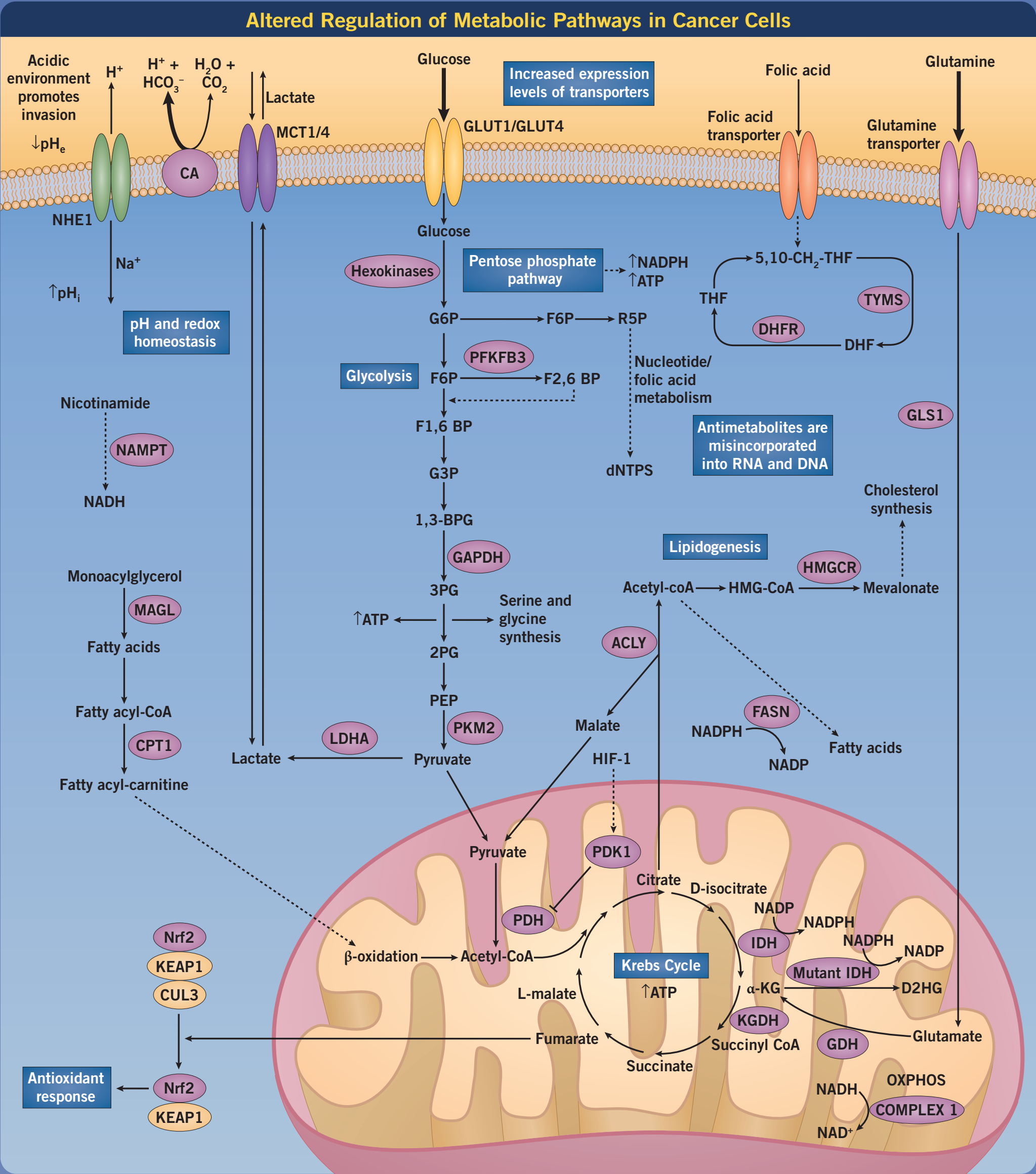
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In 1924 Otto Warburg first discovered that cancer cells generated a large proportion of their ATP by metabolizing glucose via aerobic glycolysis (as opposed to mostly through oxidative phosphorylation (OXPHOS) in normal cells). Initially it was thought that this Warburg effect was a cause of cancer, but it was later established that this shift to glycolytic metabolism was an effect of cancer cell transformation. Genetic changes and epigenetic modifications in cancer cells alter the regulation of cellular metabolic pathways. These distinct metabolic circuits could provide viable cancer therapeutic targets.



**pH and Redox Balance**

Cancer cells are able to survive in their hostile microenvironments because of increased expression of proton pumps and ion transporters. Aberrant regulation of hydrogen ions leads to a reversal of the pH gradient across tumor cell membranes, resulting in a more basic intracellular pH (pH<sub>i</sub>) and a more acidic extracellular pH (pH<sub>e</sub>). It is critical to cancer cell survival that the intracellular environment does not become acidified because this could induce apoptosis.



ACLY, ATP citrate lyase; ATP, Adenosine triphosphate; 1,3-BPG 1,3-Bisphosphoglyceric acid; CA, carbonic anhydrase; CPT1, carnitine palmitoyltransferase; CUL3, Cullin 3; D2HG, D-2-hydroxyglutarate; DHF, dihydrofolate; DHFR, DHF reductase; FASN, fatty acid synthase; F1,6BP, fructose-1,6-bisphosphate; F2,6BP, fructose-2,6-bisphosphate; F6P, fructose-6-phosphate; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; GDH, glutamate dehydrogenase; GLUT, glucose transporter; GLS1, glutaminase; G3P, Glyceraldehyde-3-phosphate; G6P, glucose-6-phosphate; HIF-1, Hypoxia-inducible factor 1; HMGCR, HMG-CoA reductase; IDH, isocitrate dehydrogenase; α-KG, α-ketoglutarate; KGDH, α-ketoglutarate dehydrogenase; LDHA, lactate dehydrogenase A; MAGL, monoacylglycerol lipase; MCT, monocarboxylate transporter; NAD<sup>+</sup>/NADH, Nicotinamide adenine dinucleotide (oxidised/reduced forms respectively); NADPH, Nicotinamide adenine dinucleotide phosphate; NAMPT, nicotinamide phosphoribosyltransferase; Nrf2, Nuclear factor (erythroid-derived 2)-like 2; OXPHOS, oxidative phosphorylation; PDH, pyruvate dehydrogenase; PDK, pyruvate dehydrogenase kinase; PEP, phosphoenolpyruvate; PFKFB3, 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase; 2PG, 2-phosphoglycerate; 3PG, 3-phosphoglycerate; PKM2, pyruvate kinase M2 isoform; PPP, Pentose Phosphate Pathway; ROS, reactive oxygen species; R5P, ribose-5-phosphate; 5,10-CH<sub>2</sub>-THF, 5,10-methylene tetrahydrofolate; THF, tetrahydrofolate; TYMS, thymidylate synthase.

Products available from Tocris
ATP-citrate Lyase (ACLY) BMS 303141, SB 204990
Carbonic Anhydrases (CA) Topiramate, U 104
Carnitine Palmitoyltransferase (CPT) (R)-(+)-Etomoxir
Dihydrofolate Reductase CI 898, Methotrexate
Fatty Acid Synthase (FASN) C 75, Orlistat
GAPDH CGP 3466B
Glucose Transporters (GLUT) STF 31
Glutaminase (GLS1) 968
Glutathione S-transferase CRID3 sodium salt
Hexokinase GKA 50, Lonidamine
HMG-CoA Reductase (HMG-CoA) Atorvastatin, Pitavastatin calcium
Lactate Dehydrogenase A (LDHA) GSK 2837808A
Monoacylglycerol Lipase (MAGL) JJKK 048, JW 642, JZL 184, JZL 195, KML 29
Monocarboxylate Transporters (MCTs) AR-C155858, CHC, UK 5099
MutT homolog-1 (MTH1) SCH 51344
NAMPT FK 866, GPP 78, STF 118804
Na <sup>+</sup> /H <sup>+</sup> Exchanger (NHE) Cariporide, EIPA, Zoniporide
Nrf2 CDDO Im, NK 252, TAT 14
Oxidative Phosphorylation (OXPHOS) Rotenone
PFKFB3 3PO, PFK 15, YZ9
Pyruvate Dehydrogenase (PDH) CPI 613
Pyruvate Dehydrogenase Kinase (PDK) DCA
Pyruvate Kinase M2 (PKM2) ML 202
Ribonucleotide Reductase Gemcitabine hydrochloride
Thymidylate Synthetase Flouxuridine, 5-Fluorouracil, Trifluorothymidine

**References:**  
Butler *et al* (2013) Stalling the engine of resistance: targeting cancer metabolism to overcome therapeutic resistance. *Cancer Res.* 73 2709.  
Chartoumpakis *et al* (2015) Keap1/Nrf2 pathway in the frontiers of cancer and non-cancer cell metabolism. *Biochem. Soc. Trans.* 43 639.  
Doherty *et al* (2014) Blocking lactate export by inhibiting the Myc target MCT1 disables glycolysis and glutathione synthesis. *Cancer Res.* 74 908.  
Feng *et al* (2012) Dysregulated lipid metabolism in cancer. *World J. Biol. Chem.* 3 167.  
Galluzzi *et al* (2013) Metabolic targets for cancer therapy. *Nat. Rev. Drug Discov.* 12 829.  
Pavlova and Thompson (2016) The emerging hallmarks of cancer metabolism. *Cell Metab.* 23 27.

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