

When levels of carbohydrates in the body significantly drops, the cell must find a way to synthesize glucose out of non-carbohydrate precursors. This process is called gluconeogenesis and occurs during periods of prolonged starvation. In this process the Krebs cycle becomes a busy avenue where carbon skeletons of glucogenic amino acids enter and are used to form pyruvate. Gluconeogenesis seems to be a reversed glycolytic pathway, yet three steps should be bypassed through other enzymes in different departments of the cell namely the mitochondrion. These are the steps catalyzed by pyruvate carboxylase and pyruvate kinase. These are the most exergonic processes in glycolysis. Generation of glucose starts with the conversion of pyruvate into phosphoenolpyruvate by pyruvate carboxylase (PC) in the mitochondrion. This reaction requires ATP and a Magnesium ion as a cofactor. Since PC is located in the mitochondrion could not traverse the mitochondrial membrane, it is turned into malate by malate dehydrogenase. Malate then exits the mitochondrion and is reconverted to oxaloacetate for gluconeogenesis. The succeeding reactions are just the reverse of the glycolytic pathway up until Fructose-1,6-bisphosphate is formed. Dephosphorylation is then facilitated by Fructose-1,6-

bisphosphatase, an endergonic reaction that requires 16.7 kJ/mol (4.0 kcal/mol) and yield Fructose-6-phosphate that further isomerizes to Glucose-6-phosphate. In liver cells where majority of gluconeogenesis occurs, Glucose-6-phosphate is further dephosphorylated to form glucose that is released from the cell for consumption of other cells in the body.