1. Record Nr. UNINA9910136401603321

Autore	Schurr A (Avital)
Titolo	Glycolysis at 75: Is it time to tweak the first elucidated metabolic pathway in history?
Pubbl/distr/stampa	Frontiers Media SA, 2015
Descrizione fisica	1 online resource (126 p.)
Collana	Frontiers Research Topics
Soggetti	Medicine
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia

Sommario/riassunto

Glycolysis, the pathway of enzymatic reactions responsible for the breakdown of glucose into two trioses and further into pyruvate or lactate, was elucidated in 1940. For more than seven decades, it has been taught precisely the way its sequence was proposed by Embden, Meyerhof and Parnas. Accordingly, two outcomes of this pathway were proposed, an aerobic glycolysis, with pyruvate as its final product, and an anaerobic glycolysis, identical to the aerobic one, except for an additional reaction, where pyruvate is reduced to lactate. Several studies in the 1980s have shown that both muscle and brain tissues can oxidize and utilize lactate as an energy substrate, challenging this monocarboxylate's reputation as a useless end-product of anaerobic glycolysis. These findings were met with great skepticism about the idea that lactate could be playing a role in bioenergetics. In the past quarter of a century monocarboxylate transporters (MCTs) were identified and localized in both cellular and mitochondrial membranes. A lactate receptor has been identified. Direct and indirect evidence now indicate that the enzyme lactate dehydrogenase (LDH) resides not only in the cytosol, as part of the glycolytic pathway machinery, but also in the mitochondrial outer membrane. The mitochondrial form of the enzyme oxidizes lactate to pyruvate and concomitantly produces the reducing agent NADH. These findings have shed light on a major drawback of the originally proposed aerobic version of the glycolytic pathway i.e., its inability to regenerate NAD+, as opposed to anaerobic

glycolysis that features the cyclical ability of regenerating NAD+ upon pyruvate reduction to lactate by the cytosolic form of LDH. The malate-aspartate shuttle (MAS), a major redox shuttle in the brain, was proposed as an alternative pathway for NAD+ generation for aerobic glycolysis. Nonetheless, would MAS really be necessary for that function if glycolysis always proceeds to the end-products, lactate and NAD+? An additional dilemma the originally proposed aerobic glycolysis presents has to do with the glycolytic pathway of erythrocytes, which despite its highly aerobic environment, always produces lactate as its end-product. It is time to reexamine the original, dogmatic separation of glycolysis into two distinct pathways and put to test the hypothesis of a unified, singular pathway, the end-product of which is lactate, the real substrate of the mitochondrial TCA cycle.