The COVID pandemic resolves the two and half centuries mystery of lactic acid in cell metabolism

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Abstract

Lavoisier defined respiration as combustion of nutrients by oxygen (O2) and Scheele discovered lactic acid in 18th century. Berzelius, Liebig, Scherer, and Fletcher in 19th century reported lactic acid accumulates in the dead tissues during rigor mortis. Pasteur (1860) reported Yeast ferment sugars to alcohol in anerobic conditions; lactic acid contamination suspends fermentation in aerobic conditions and promotes growth of Yeast. Harden and Young (1906-1914) reported that thermostable cofactor and Pi in cell free extracts of Yeast stabilize hexose diphosphate and promote alcohol production. Harden's model is the origin of present models of intermediary metabolism. Meyerhof proposed muscles convert glycogen to lactic acid during contraction. Warburg discovered two thermostable cofactors NAD+ and NADP+. Besides, Warburg proposed "Pasteur effect" to suggest O2 inhibits glycolysis, and "aerobic glycolysis" to suggest cancer cells have damaged mitochondria and produce lactic acid in the presence of O2. Brooks, Gladden and Sonveaux in the past six decades reported that lactic acid entry into cells activates pyruvate metabolism and mitochondrial respiration in muscles and cancers. Enhanced utilization of fructose rich diets cause disturbances in the glycemic index and cause insulin resistance is reported by several authors. Besides, several glycolytic enzymes are reported to exhibit non-canonical moonlighting functions. Several recent studies indicate lactic acid produced by gut microbes inhibits immune checkpoints and promotes survival pathways in cancers. Studies on Covid-19 infections suggest that obese, diabetes, and aged patients, with diminished lactic acid circulation are susceptible to infections. It is proposed that activation of fructose transporter (SLC2A5) promotes uptake of essential amino acids and regulates hexose phosphate shuttles, Oxidation of phosphoglycerates promotes ATP and nucleotide production. Lactic acid produced by gut microbes promotes pyruvate metabolism. ATP hydrolysis / export out of cells and peroxisomal acyl/acetyl-CoA synthesis promote mitochondrial respiration and glutamine metabolism and cell growth.

Biography

Lakshmipathi Vadlakonda was completed his MSc (1970), Osmania University, Hyderabad, PhD (1982) (Kakatiya University Warangal). He worked as a Faculty Member in CKM College (1971-1980). Kakatiya University, 506009 (1980-2006; Retired as Professor and Head in 2006). Post retirement (2006-2010): Visiting professor in HCU and NIPER, Hyderabad. Adjunct professor, CR RAO institute of AIMSCS, Consultant scientist, Cell Works Bangalore. Present: Independent researcher (works from home): Examines emerging and classical literature on cell signaling, metabolic regulation and pathology of diabetes, and cancer.

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