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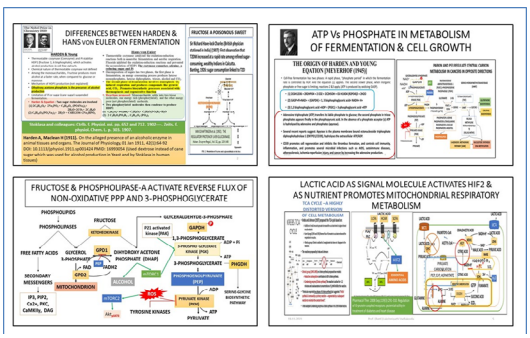
Revisiting the intermediary metabolism-ignored reports and biased hype on bioenergetics need a fresh look

Present models of intermediary metabolism were based on Pasteur's experiments on Yeast. Pasteur demonstrated that Yeast produce alcohol under anaerobic conditions and lactic acid contamination suspends fermentation and promotes growth. Buchner demonstrated that zymase (enzymes) in cell free extracts produces alcohol. Harden discovered thermostable cofactor and Pi stabilize the Hexose diphosphate (HDP) and that dihydroxyacetone phosphate (DHAP) is the precursor of alcohol production. In parallel studies, Hans von Euler reported that the thermostable cofactor activates several oxidative-reductive reactions and partitioned chemical reactions into anaerobic fermentation and respiration dependent biosynthesis programmes, which promote thermogenesis and tissue regeneration. Stoklasa reported human tissues produce alcohol and Havelock-Charles reported refined cane sugar contributed to type-2 diabetes and obesity. Post 1940s, Meyerhof altered his opinion on glycolysis. In a revisit to Harden and Young equation, Meyerhof (1945) proposed that PGK1 produces ATP and apyrase hydrolyses ATP to stabilise the Harden ester. Several recent reports suggest that fructose metabolism activates fermentation, and lactic acid as a paracrine fuel activates oxidative mitochondrial metabolism.



Hypothesis: Fructose inhibits glucose uptake and activates cell metabolism to repopulate mesenchymal cells. Pi dependent anaerobic breakdown of glycogen coupled with the hydrolysis of collagen by the mesenchymal cells liberates proline and non-essential amino acids. TGFβ1 inhibits the cotransporter 4F2HC (CD38). Glutamine entry into cells shuttles fructose-6 phosphate into hexosamine biosynthetic pathway which activates 4F2HC. By binding to cysteine transporterSLC7A11 (xCT) and the LAT1 transporter; 4F2HC activates uptake of cysteine and the essential amino acids. Aconitase1 partitions the anaerobic and aerobic metabolism by activating the cyanide resistant respiration in cells. Lactic acid can be produced from the alcohol by activating the alcohol dehydrogenase or by cyanide dependent glycerol conversion to lactic acid, which requires the zerovalent iron.

Speaker Biography

Lakshmipathi Vadlakonda has completed his PhD in 1982 from Kakatiya University, India. He has been the Faculty of Kakatiya University from 1971 to 2006 (till his retirement) and after retirement he served as a Visiting Professor, University of Hyderabad, a Consultant Scientist at Cell works, Bangalore, Guest Professor at NIPER Hyderabad and as Adjunct Professor at CRRAO (AIMS). He has 45 years of teaching experience; mainly in the areas cell biology, enzymology and metabolic regulation. His focus after retirement for the past 8 years is on cell signaling in cancer and diabetes.

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