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| Nota di contenuto       | GAPDH: Biological Properties and Diversity; Contents; Introduction; Chapter 1: Basic Biology of GAPDH; 1.1 The GAPDH Gene; 1.1.1 Coding Region; 1.1.2 Promoter Sequence; 1.1.2.1 Hypoxia-Responsive Elements; 1.1.2.2 Basal Level Expression; 1.1.2.3 Glutamine-Responsive Elements; 1.1.3 Testes-Specific Isoform; 1.1.4 GAPDH Pseudogenes; 1.2 Regulation of GAPDH Expression; 1.2.1 Tissue Specificity; 1.2.2 Tracking GAPDH Information Electronically; 1.2.3 Cancer; 1.3 Cellular Levels of GAPDH; 1.4 Oxidoreductase Activity of GAPDH; 1.4.1 Mechanism of Catalysis; 1.4.2 Kinetic Parameters 1.5 Architecture of the GAPDH Protein 1.5.1 Asymmetric Homotetramer; 1.5.2 Dinucleotide Binding Domain; 1.5.3 Catalytic Domain; References; Chapter 2: GAPDH and Intermediary Metabolism; 2.1 GAPDH, the Glycolytic Lynch-Pin; 2.1.1 Metabolic Switch; 2.1.2 Glycolytic Tissues; 2.1.3 Anaerobic Glycolysis; 2.2 Determining GAPDH Activity; 2.2.1 Chemical Inhibitors; 2.2.2 Measurement of Glycolytic Flux; 2.2.3 Oxidoreductase Activity of GAPDH; 2.2.3.1 Conditions of Assay; Buffer Selection; Triethanolamine Buffer; Sodium Phosphate Buffer; GAPDH (rabbit muscle); Reagents; NAD <sup>+</sup> stock solution (10mM) d/l-glyceraldehyde stock solution (200mM) 2.2.3.2 Assay Protocol; |

Determine Rate of NAD<sup>+</sup> Reduction; Calculate Specific Activity; 2.3 Role of GAPDH Metabolites; 2.3.1 Counter-Catalytic Activity; 2.3.2 Controlling NADH Levels; 2.3.3 Phosphocreatine, as a Competitive Inhibitor; 2.3.4 Metabolic Parameters in the Brain; 2.4 Comparative Analysis; 2.4.1 Structure-Function of NAD<sup>+</sup>-Binding; 2.4.2 Sequence Homology; References; Chapter 3: Compartmentation of GAPDH; 3.1 Compartmentation of Glycolytic Energy; 3.1.1 Microzones of Cellular ATP; 3.1.2 Focal Regulation of NAD<sup>+</sup>/NADH Ratios; 3.1.3 Channeling of Metabolites; 3.1.4 Non-glycolytic Compartmentation; 3.2 Binding to the Plasma Membrane; 3.2.1 SLC4 Anion Exchanger; 3.2.1.1 Band 3 in Erythrocytes; 3.2.1.2 Kidney AE1 Isoform; 3.2.2 Na<sup>+</sup>/K<sup>+</sup>-ATPase; 3.2.3 ATP-Sensitive K<sup>+</sup>-Channel; 3.2.4 GLUT Transporters; 3.2.4.1 GLUT1 Transporter in Erythrocytes; 3.2.4.2 GLUT4 Transporter; 3.2.5 GABA (Type A) Receptor; 3.2.6 GAPDH, as a Lactoferrin Receptor; 3.3 Translocation to the Nucleus; 3.4 Other Non-cytosolic Destinations; 3.4.1 Clathrin-Coated Vesicles; 3.4.2 Golgi Apparatus and Endoplasmic Reticulum; 3.4.3 Sarcoplasmic Reticulum; 3.4.4 Mitochondria; 3.5 Dendrites, Axons and Synapses; 3.5.1 Synaptic Vesicles; 3.5.2 Post-synaptic Density; 3.6 Specialized Compartment for Spermatogenic GAPDH; References; Chapter 4: Functional Diversity; 4.1 Classical Example of Protein 'Moonlighting'; 4.1.1 Evolutionary Considerations; 4.1.2 Molecular Mechanisms; 4.2 Structural Organization of the Cell; 4.2.1 Cytoskeletal Components; 4.2.1.1 Actin Filaments; 4.2.1.2 Microtubules; 4.2.2 Organelle Biogenesis; 4.2.2.1 Triadic Junction; 4.2.2.2 Nuclear Envelope; 4.2.2.3 Vesicle Recycling/Membrane Fusion; 4.2.2.4 Cell Polarization; 4.2.2.5 Golgi and Endoplasmic Reticulum

## Sommario/riassunto

GAPDH (glyceraldehyde 3-phosphate dehydrogenase) is more than just a glycolytic enzyme. An unprecedented amount of literature demonstrates that GAPDH has an astounding multiplicity of function. This diversity is not simply due to cell compartmentation (i.e. redistributing glycolytic energy to where it is needed), although this feature is undoubtedly important and discussed in the book. GAPDH integrates glycolysis with other cellular processes. This concept of integration cannot be understated. But, there is more. GAPDH actively participates in numerous non-glycolytic cellular events that fall into very broad categories including the cell infrastructure and the transmission of genetic information. Some of GAPDH's biological properties are completely non-intuitive given the current undergraduate textbook understanding of this glycolytic enzyme. For example, GAPDH binds to select phospholipids and catalyzes organelle biogenesis. It has fusogenic properties, enabling it to be actively involved in nuclear envelop reassembly, autophagy and membrane trafficking. Human macrophages exhibit surface-localized GAPDH with receptor function. As scientists, we are trained to consider GAPDH as a soluble cytosolic dehydrogenase enzyme. The literature observations - as described in this book - tell us something quite different. Besides oxidoreductase activity, GAPDH exhibits peroxidase, uracil DNA glycosylase, nitrosylase, mono-ADP-ribosylase, esterase and phosphotransferase activity. GAPDH binds membrane transport proteins, G-proteins, poly-nucleotides, adenines, specific lipids, select carbohydrates, cytoskeletal proteins, nuclear import and export proteins, diverse ATPases, molecular chaperones and other molecules.