Postgraduate Certificate in Advanced Nutritional Biochemistry

Molecular Nutrition and Metabolism

Adenosine Triphosphate (ATP) – The universal cellular energy currency that drives endergonic reactions. Related terms: ADP, phosphocreatine, oxidative phosphorylation. ATP is regenerated principally through mitochondrial respiration and substrate-level phosphorylation. Practical application includes assessing cellular energy status in muscle biopsies of athletes. A major challenge is the rapid degradation of ATP ex vivo, requiring immediate quenching techniques.

Beta-Oxidation – The mitochondrial pathway that catabolises long-chain fatty acids into acetyl-CoA units. Related terms: Carnitine shuttle, Acyl-CoA dehydrogenase, ketogenesis. Example: increased beta-oxidation rates observed in fasting rodents. Clinically, measuring β-oxidation capacity helps evaluate metabolic flexibility in obese patients. Inhibitors such as etomoxir illustrate the difficulty of selectively targeting this pathway without off-target effects.

Carnitine Shuttle – A transport system that translocates long-chain acyl groups across the inner mitochondrial membrane. Related terms: CPT-I, CPT-II, carnitine palmitoyltransferase. Deficiencies can cause muscle weakness and hypoketotic hypoglycemia. Supplementation studies show mixed results on enhancing fatty-acid oxidation during endurance exercise, highlighting variability in individual response.

DNA Methylation – An epigenetic modification involving the addition of a methyl group to cytosine residues, influencing gene expression. Related terms: CpG islands, epigenomics, methyltransferases. Nutrients such as folate and betaine serve as methyl donors, linking diet to epigenetic regulation. Analytical challenges include distinguishing 5-methylcytosine from oxidized derivatives in bisulfite sequencing.

Enzyme Kinetics – The quantitative study of enzyme-catalyzed reaction rates and their dependence on substrate concentration. Related terms: Michaelis-Menten constant (Km), Vmax, allosteric regulation. Example: measuring hexokinase activity in liver homogenates to assess glycolytic flux. Accurate kinetic parameters require careful control of temperature, pH, and cofactor concentrations.

Fatty Acid Synthase (FAS) – A multifunctional enzyme complex that catalyses de novo synthesis of palmitate from acetyl-CoA and malonyl-CoA. Related terms: Lipogenesis, ACC, malonyl-CoA. Overexpression of FAS is a hallmark of many cancers, making it a therapeutic target. Inhibitors often suffer from poor specificity, underscoring the need for selective drug design.

Glucose Transporter Type 4 (GLUT4) – An insulin-responsive facilitative transporter that mediates glucose uptake into skeletal muscle and adipose tissue. Related terms: Insulin signaling, Akt, translocation. Exercise-induced GLUT4 translocation occurs independently of insulin, offering a strategy to improve glycaemic control in insulin-resistant individuals. Quantifying GLUT4 membrane insertion remains

technically demanding.

Hormone-Sensitive Lipase (HSL) – A key lipase that hydrolyses stored triacylglycerols in adipocytes during fasting or catecholamine stimulation. Related terms: PKA, lipid droplets, adipose tissue. Phosphorylation of HSL enhances its activity, while insulin promotes its dephosphorylation. Dysregulated HSL activity contributes to ectopic lipid accumulation, a challenge for metabolic disease research.

Insulin – A peptide hormone secreted by pancreatic β-cells that regulates carbohydrate, lipid, and protein metabolism. Related terms: Glucagon, insulin receptor, PI3K-Akt pathway. Acute insulin infusion lowers plasma free fatty acids, illustrating its antilipolytic effect. Chronic hyperinsulinaemia leads to receptor down-regulation, complicating therapeutic interventions.

Ketogenesis – The hepatic synthesis of ketone bodies (β-hydroxybutyrate, acetoacetate) from acetyl-CoA during carbohydrate restriction. Related terms: HMG-CoA synthase, ketogenic diet, energy substrate. Ketone bodies serve as alternative fuels for brain and muscle during prolonged fasting. Measuring ketone turnover requires stable-isotope tracer techniques, which are costly and technically intensive.

Lipidomics – The large-scale study of cellular lipid species using mass spectrometry-based platforms. Related terms: Phospholipids, sphingolipids, shotgun lipidomics. Lipidomic profiling of plasma can reveal biomarkers of cardiovascular risk. Data analysis is hampered by isobaric species and the need for robust annotation pipelines.

Metabolomics – The comprehensive analysis of low-molecular-weight metabolites in biological samples. Related terms: NMR spectroscopy, LC-MS, metabolic fingerprinting. Metabolomic signatures differentiate responders from non-responders to dietary interventions. Standardisation of sample collection and storage remains a major barrier to reproducibility.

NAD^+ (Nicotinamide Adenine Dinucleotide) – A redox cofactor central to oxidative metabolism and signalling pathways. Related terms: Sirtuins, PARPs, NAD^+ salvage pathway. Boosting NAD^+ levels with precursors such as nicotinamide riboside improves mitochondrial function in aged mice. Human trials show variable bioavailability, indicating a gap between preclinical and clinical outcomes.

Omega-3 Fatty Acids – Polyunsaturated fatty acids (e.g., EPA, DHA) that modulate inflammation and membrane fluidity. Related terms: Eicosapentaenoic acid, docosahexaenoic acid, omega-6/omega-3 ratio. Supplementation reduces triglyceride concentrations, yet inter-individual variability in response complicates dose recommendations. Oxidative stability of fish oil supplements is a practical concern.

Phospholipid Remodeling – The enzymatic turnover of fatty acyl chains on phospholipids, affecting membrane composition. Related terms: Lands' cycle, PLA_2, acyl-CoA synthetase. Altered remodeling is linked to insulin resistance in skeletal muscle. Quantifying specific phospholipid species demands high-resolution MS and careful lipid extraction protocols.

Quercetin – A flavonoid antioxidant found in fruits and vegetables, influencing cellular signalling. Related terms: Polyphenols, ROS scavenging, NF-κB inhibition. In vitro, quercetin activates AMPK, enhancing glucose uptake. However, poor intestinal absorption limits its efficacy in vivo, prompting research into nano-formulations.

Reactive Oxygen Species (ROS) – Chemically reactive molecules derived from oxygen, such as superoxide and hydrogen peroxide. Related terms: Antioxidant defenses, oxidative stress, redox signalling. Moderate ROS levels act as second messengers, while excess leads to lipid peroxidation. Accurate quantification requires probes that avoid artefactual generation during sample handling.

Sirtuins – NAD^+-dependent deacetylases that regulate metabolic pathways and longevity. Related terms: SIRT1, mitochondrial biogenesis, caloric restriction. Activation of SIRT1 by resveratrol improves insulin sensitivity in animal models, yet human trials yield inconsistent results due to dosage and bioavailability issues.

Transporter Proteins – Membrane-embedded proteins that facilitate the movement of solutes across cellular barriers. Related terms: ABC transporters, solute carriers, substrate specificity. Example: the amino acid transporter LAT1 mediates leucine uptake, influencing mTOR signalling. Overexpression of certain transporters in tumors poses challenges for targeted drug delivery.

Urea Cycle – A hepatic pathway that converts ammonia to urea for excretion. Related terms: Ornithine transcarbamylase, argininosuccinate lyase, hyperammonemia. Dietary protein excess increases urea cycle flux, measurable by stable-isotope tracing. Genetic deficiencies result in life-threatening metabolic crises, highlighting the need for early detection.

Vitamin D Metabolism – The conversion of cholecalciferol to active 1,25-dihydroxyvitamin D via hepatic 25-hydroxylation and renal 1α-hydroxylation. Related terms: Calcium homeostasis, VDR, photolysis. Vitamin D status influences muscle function and insulin secretion. Determining optimal serum 25-hydroxy-vitamin D levels for metabolic health remains controversial.

Water-Soluble Vitamins – Vitamins that dissolve in aqueous media and act as co-enzymes in metabolic reactions. Related terms: B-complex, vitamin C, renal excretion. Thiamine (B1) is essential for pyruvate dehydrogenase activity; deficiency leads to lactic acidosis. Water-soluble vitamins are generally excreted rapidly, requiring regular dietary intake.

Xanthine Oxidase – An enzyme that catalyses the oxidation of hypoxanthine to xanthine and then to uric acid, generating ROS as by-products. Related terms: Purine catabolism, allopurinol, gout. Inhibition of xanthine oxidase reduces oxidative stress in endothelial cells, yet long-term therapy can precipitate hypersensitivity reactions, underscoring risk-benefit considerations.

Yeast One-Hybrid Assay – A molecular technique used to study protein-DNA interactions relevant to nutrient-responsive transcription factors. Related terms: Transcriptional activation, reporter gene,

electrophoretic mobility shift assay. This assay helps identify binding sites of carbohydrate-responsive element-binding protein (ChREBP). Limitations include potential artefacts from heterologous expression systems.

Zinc Homeostasis – The regulated balance of intracellular and extracellular zinc, crucial for enzymatic catalysis and transcription factor function. Related terms: Metallothioneins, ZIP transporters, ZnT proteins. Zinc deficiency impairs insulin synthesis, while excess interferes with copper absorption. Accurate measurement of labile zinc pools requires fluorescent probes with high specificity.

Acetyl-CoA Carboxylase (ACC) – The rate-limiting enzyme of de novo fatty-acid synthesis, converting acetyl-CoA to malonyl-CoA. Related terms: Malonyl-CoA, AMPK, fatty-acid synthase. Pharmacological ACC inhibition lowers hepatic lipid accumulation, offering a therapeutic avenue for non-alcoholic fatty liver disease. Isoform-specific effects and compensatory pathways present ongoing challenges.

Branched-Chain Amino Acid (BCAA) Metabolism – The catabolic pathway for leucine, isoleucine, and valine, involving transamination and oxidative decarboxylation. Related terms: BCKDH complex, mTOR activation, insulin resistance. Elevated circulating BCAAs correlate with type 2 diabetes risk, yet mechanistic causality remains debated. Tissue-specific flux analysis is required to dissect hepatic versus muscle contributions.

Coenzyme Q10 (Ubiquinone) – A lipid-soluble electron carrier within the mitochondrial respiratory chain and an antioxidant. Related terms: Complex III, oxidative phosphorylation, ubiquinol. Supplementation improves mitochondrial efficiency in patients with primary CoQ10 deficiency. Bioavailability is limited by its hydrophobic nature, prompting formulation research.

De Novo Lipogenesis (DNL) – The synthesis of fatty acids from non-lipid precursors, primarily carbohydrates, in the liver and adipose tissue. Related terms: Acetyl-CoA, fatty-acid synthase, insulin. High-fructose diets stimulate DNL, contributing to hepatic steatosis. Quantifying DNL in humans often relies on isotopic tracer methods, which are resource-intensive.

Electron Transport Chain (ETC) – A series of membrane-embedded complexes (I-IV) that transfer electrons from NADH and $FADH_2$ to oxygen, generating a proton motive force. Related terms: Oxidative phosphorylation, ATP synthase, mitochondrial membrane potential. Dysfunction of Complex I is implicated in neurodegenerative diseases. High-resolution respirometry enables functional assessment but requires fresh tissue.

Folate Cycle – An interlinked set of reactions that transfer one-carbon units for nucleotide synthesis and methylation reactions. Related terms: 5-MTHF, homocysteine, methionine cycle. Folate deficiency elevates homocysteine, a risk factor for cardiovascular disease. Dietary folate fortification has reduced neural-tube defects, yet excess intake may mask vitamin B12 deficiency.

Glutathione (GSH) – A tripeptide (γ-glutamyl-cysteinyl-glycine) that serves as the principal cellular antioxidant and redox buffer. Related terms: GSSG, glutathione peroxidase, Nrf2. GSH depletion is observed

in oxidative-stress-related disorders such as diabetes. Restoring GSH levels through N-acetylcysteine supplementation is limited by transport and synthesis capacity.

Hexokinase II – The isoform of hexokinase that phosphorylates glucose in muscle and adipose tissue, coupling glycolysis to ATP production. Related terms: Glycolytic flux, mitochondrial binding, Warburg effect. Overexpression in cancer cells promotes high glycolytic rates. Inhibition studies must account for compensatory activity of other hexokinase isoforms.

Iron-Sulfur Cluster Biogenesis – The assembly of Fe-S cofactors essential for enzymes involved in electron transport and DNA repair. Related terms: ISC machinery, mitochondrial matrix, aconitase. Mutations in ISC assembly proteins cause sideroblastic anemia and neurodegeneration. Assessing Fe-S status in vivo remains technically demanding.

JAK-STAT Signalling – A cytokine-mediated pathway that transduces extracellular signals to the nucleus, influencing metabolic gene expression. Related terms: Leptin receptor, SOCS proteins, transcriptional regulation. Dysregulated JAK-STAT activity contributes to chronic inflammation in obesity. Pharmacological JAK inhibitors improve inflammatory profiles but may affect glucose homeostasis.

Krebs Cycle (Citric Acid Cycle) – The central metabolic hub that oxidises acetyl-CoA to CO_2, producing NADH, $FADH_2$, and GTP. Related terms: Anaplerosis, succinate dehydrogenase, oxaloacetate. Intermediates serve as precursors for amino-acid synthesis. Flux analysis using ^13C-labelled substrates provides insight into metabolic rewiring in disease.

Lactate Shuttle – The concept that lactate produced in glycolytic fibers is exported and oxidised by oxidative tissues. Related terms: Monocarboxylate transporters, Cori cycle, aerobic glycolysis. Elevated lactate during high-intensity exercise reflects efficient substrate utilisation. Misinterpretation of lactate as solely a waste product can hinder training optimisation.

Monocarboxylate Transporter 1 (MCT1) – A proton-coupled transporter that facilitates the influx of lactate and pyruvate into oxidative cells. Related terms: MCT4, lactate shuttle, pH regulation. Up-regulation of MCT1 in endurance training enhances oxidative capacity. Inhibitors of MCT1 are investigated as anti-cancer agents, yet systemic effects on normal metabolism must be considered.

Niacin (Vitamin B3) – A water-soluble vitamin that serves as a precursor for NAD^+ and $NADP^+$. Related terms: Nicotinic acid, pellagra, lipid-lowering effects. Pharmacological doses lower triglycerides via inhibition of hepatic diacylglycerol acyltransferase. Flushing and hepatotoxicity limit its clinical use, prompting development of flush-free analogues.

Oxidative Phosphorylation (OXPHOS) – The process by which ATP is synthesised from ADP using the proton gradient generated by the ETC. Related terms: ATP synthase, mitochondrial respiration, coupling efficiency. Mitochondrial DNA mutations impair OXPHOS, leading to metabolic myopathies. High-resolution respirometry can detect subtle OXPHOS deficits in patient biopsies.

Phosphofructokinase-1 (PFK-1) – A key regulatory enzyme of glycolysis that phosphorylates fructose-6-phosphate to fructose-1,6-bisphosphate. Related terms: Allosteric regulation, ATP inhibition, fructose-2,6-bisphosphate. In cancer cells, PFK-1 activity is up-regulated, supporting the Warburg effect. Allosteric activators are explored to boost glycolytic flux in ischemic tissues.

Quinone Redox Cycling – The process by which quinones undergo reversible reduction and oxidation, generating ROS. Related terms: Coenzyme Q10, para-benzoquinone, oxidative stress. Certain dietary polyphenols can undergo quinone cycling, contributing to both antioxidant and pro-oxidant effects. Balancing these outcomes is a key research focus.

Ribosomal Protein S6 Kinase (S6K) – A downstream effector of mTORC1 that phosphorylates the S6 ribosomal protein, promoting protein synthesis. Related terms: mTOR signalling, insulin resistance, feedback inhibition. Chronic activation of S6K contributes to serine phosphorylation of IRS-1, impairing insulin signalling. Therapeutic modulation must avoid compromising muscle protein accretion.

Signal Transducer and Activator of Transcription 3 (STAT3) – A transcription factor activated by cytokines and growth factors, influencing metabolism and inflammation. Related terms: JAK pathway, acute-phase response, mitochondrial localisation. Persistent STAT3 activation in adipose tissue drives insulin resistance. Targeted inhibition presents opportunities but risks off-target immunosuppression.

Thiamine Pyrophosphate (TPP) – The active coenzyme form of vitamin B1, required for decarboxylation reactions in carbohydrate metabolism. Related terms: Pyruvate dehydrogenase, transketolase, beriberi. TPP deficiency impairs glucose oxidation, leading to lactic acidosis. Oral supplementation restores enzyme activity but requires adequate magnesium for activation.

Ubiquitin-Proteasome System (UPS) – The cellular machinery that tags proteins with ubiquitin for degradation, regulating metabolic enzyme turnover. Related terms: E3 ligases, proteasome, protein homeostasis. In obesity, UPS-mediated degradation of insulin receptor substrate proteins contributes to insulin resistance. Proteasome inhibitors have limited use due to systemic toxicity.

Vitamin K-Dependent Carboxylation – A post-translational modification that converts glutamate residues to γ-carboxyglutamate, essential for calcium binding in clotting factors. Related terms: Phylloquinone, menaquinone, osteocalcin. Subclinical vitamin K deficiency may affect bone mineralisation and vascular health. Assessing functional status relies on measuring under-carboxylated osteocalcin levels.

Warburg Effect – The propensity of cancer cells to preferentially utilise aerobic glycolysis over oxidative phosphorylation. Related terms: Lactate production, hexokinase II, metabolic reprogramming. Exploiting the Warburg effect enables PET imaging with ^18F-FDG. Targeting glycolytic enzymes offers therapeutic promise, yet normal proliferating cells also rely on glycolysis.

X-linked Inhibitor of Apoptosis (XIAP) – A protein that blocks caspase activity, influencing cell survival and metabolic homeostasis. Related terms: Apoptosis, caspases, mitochondrial pathways. Over-expression in

tumor cells confers resistance to chemotherapeutic-induced apoptosis. Small-molecule XIAP antagonists are under investigation, but off-target toxicity remains a barrier.

Yeast Two-Hybrid System – A molecular assay used to detect protein-protein interactions relevant to metabolic signalling networks. Related terms: GAL4 DNA-binding domain, transcriptional activation, bait-prey constructs. This system identified interaction between AMPK α-subunit and LKB1, elucidating upstream activation. False positives and the requirement for nuclear localisation limit its universal applicability.

Zonulin – A protein modulating intestinal tight-junction permeability, affecting nutrient absorption and systemic inflammation. Related terms: Gut barrier, leaky gut, metabolic endotoxemia. Elevated zonulin levels correlate with obesity-related insulin resistance. Therapeutic strategies aim to normalise zonulin expression, yet measurement standardisation is lacking.