

Cellular physiology as a basis for disease mechanisms and therapeutic targets

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ABSTRACT

Cellular physiology is a crucial framework for understanding the mechanisms that maintain normal biological function and underlie disease development at the cellular level. This review aimed to synthesize current knowledge on key cellular physiological processes, including homeostasis regulation, membrane transport, signal transduction, energy metabolism, and intercellular communication, and their role in disease pathogenesis when dysfunctional. This review, which focuses on the connection between compromised cellular physiology and human disease mechanisms, employs a narrative review methodology based on the most recent scientific literature from pertinent biomedical databases. The review shows that many major diseases, such as cancer, metabolic disorders, neurodegenerative diseases, and infectious diseases, are largely caused by dysfunction in fundamental cellular processes, such as mitochondrial disorders, oxidative stress imbalance, abnormal activation of signaling pathways, and impaired cellular communication. These events are linked in intricate regulatory networks that control cell responses and destiny rather than happening in isolation. Potential therapeutic targets, including signaling molecules, metabolic regulators, ion channels, and pathways leading to programmed cell death, have been identified thanks to developments in molecular biology and systems biology. This encourages a change in treatment techniques away from only treating clinical symptoms and toward mechanism-based tactics that concentrate on reestablishing cellular equilibrium. Precision medicine and tailored therapy are based on cellular physiology, which provides a vital connection between fundamental biological systems and therapeutic applications.

Introduction

Cellular physiology is a branch of biomedical science that studies the fundamental mechanisms governing the function, behavior, and interactions of cells, the smallest structural and functional units of life (Horwitz, 2016). Its breadth includes the biophysical, biochemical, and molecular mechanisms that underlie cellular activity, such as signal transduction, membrane transport regulation, energy metabolism, and intercellular communication (Zhao *et al.*, 2026). Understanding cellular physiology is essential to comprehending how cells adapt to changes in the internal and external environment while maintaining normal function.

The ability of cells to maintain stable internal conditions through dynamic and coordinated regulatory processes is described by the idea of cellular homeostasis, which is fundamental to cell physiology (Kurniawan *et al.*, 2026). This stability includes the control of intracellular pH, ion balance, redox status, and adenosine triphosphate (ATP) availability (Wang *et al.*, 2025). Molecular sensors, signal transduction pathways, and cellular effectors are all part of the feedback system that homeostatic systems use to maintain biological processes (Valls and Esposito, 2022). When this system is disrupted, physiological abnormalities may result, which can be the beginning of a number of disease disorders (Kotas and Medzhitov, 2015).

The pathophysiology of many diseases, from metabolic and degenerative disorders to inflammatory and neoplastic disorders, has been revealed to be significantly influenced by cellular dysfunction (Liu *et al.*,

2025a). Complex clinical manifestations at the tissue and organ levels might result from cellular changes include oxidative stress, mitochondrial malfunction, signaling disruption, and cell cycle regulation failure (Azan *et al.*, 2026). Disease is therefore now understood to be the result of the failure of systemic and interrelated cellular regulatory processes rather than just an organ problem (Adrain, 2021).

Even while our understanding of the cellular mechanisms behind disease has advanced significantly, there is still a conceptual gap in the integration of cell physiology knowledge with practical therapeutic strategies (Su *et al.*, 2024). Without taking into account the intricacy of the interacting cellular regulatory networks, the majority of treatment interventions continue to concentrate on single molecular targets (Onose *et al.*, 2022). This reductionistic approach frequently leads to therapeutic efficacy limitations, such as the development of resistance, adverse effects, and persistent nonresponsiveness (Duval, 2018). Thus, an integrative paradigm that links mechanism-based treatment design with cellular physiology principles is required (Bassingthwaighte, 2010).

With the advancement of analytical tools like systems biology and omics, which allow for more thorough mapping of cellular networks, the necessity of this integration is growing (Dai and Shen, 2022). This method makes it possible to see disease as the outcome of intricate biological systems malfunctioning rather of just alterations in a single molecular component (Ali, 2023). Therefore, cellular physiology can provide a conceptual basis for the creation of treatment approaches that are more accurate, flexible, and systems-based (Thomas, 2022).

The purpose of this review was to present a comprehensive synthesis of the principles of cellular physiology and their relationship to disease mechanisms, and to explore how dysfunction at the cellular level contributes to various pathological conditions. Additionally, by highlighting the possible integration of cellular biology, systems biology, and contemporary technology in the creation of next-generation medical interventions, this review seeks to find therapeutic approaches based on an understanding of cellular physiology. Therefore, it is anticipated that this article will offer a conceptual framework that fortifies the connection between the scientific underpinnings of cellular physiology and more successful therapeutic applications.

Fundamental principles of cellular physiology

Cellular physiology is based on the fundamental principles that govern the internal stability of cells and the coordination of various biological processes that enable cells to maintain normal function and respond adaptively to environmental changes. The integrated relationship among homeostasis, membrane transport, signal transduction, and energy metabolism is illustrated in Figure 1.

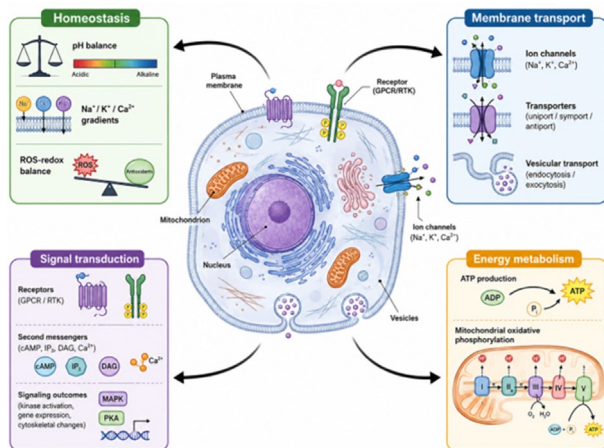


Figure 1. Integrated framework of cellular physiology in maintaining homeostasis.

Cellular homeostasis

A key concept in cell physiology is cellular homeostasis, which describes a cell's capacity to sustain steady internal conditions in spite of changes in the external environment (Billman, 2020). This stability is essential for maintaining the cell's general survival, structural integrity, and metabolic activity (Fulda *et al.*, 2010). Complex coordination between sensory systems, signal transduction pathways, and molecular effectors—all of which function in a dynamic and integrated way—is required for homeostatic regulation (Hotamisligil and Davis, 2016).

The control of intracellular pH and ionic balance is an essential component of cellular homeostasis (Pittman, 2012). Membrane transporters and energy-dependent ion pumps, such as Na^+/K^+ -ATPase and Ca^{2+} -ATPase, are responsible for maintaining ion gradients of sodium, potassium, calcium, and chloride (Contreras *et al.*, 2024). In addition to being essential for preserving membrane potential, these gradients are involved in a number of physiological functions, including secretion, cell contraction, and signal transmission (Mahapatra *et al.*, 2025). Additionally, buffer systems, proton transporter activity, and bicarbonate ion exchange all work together to keep intracellular pH within a specific range, ensuring enzyme stability and preventing protein denaturation (Shaw and Gregory, 2022).

Energy balance is another essential element from a metabolic standpoint (Sautchuk and Eliseev, 2022). Through metabolic processes like glycolysis, the citric acid cycle, and oxidative phosphorylation, cells constantly modify the synthesis and consumption of ATP (Bonora *et al.*, 2012). Adenosine monophosphate-activated protein kinase (AMPK) and other

cellular energy sensors are involved in identifying shifts in energy status and triggering adaptive reactions, such as enhanced catabolism and inhibited anabolic processes (Garcia and Shaw, 2017). Many clinical illnesses, like as metabolic and degenerative disorders, are frequently linked to dysfunction in this energy control (Bhatti *et al.*, 2017).

In addition to preserving basal conditions, cells may adjust to a variety of stressors, including chemical, biological, and physical ones (Zhang *et al.*, 2008). In order to combat oxidative stress, stress responses include the activation of defense mechanisms such the unfolded protein response (UPR), the heat shock response, and antioxidant systems (Ulfig and Jakob, 2024). These reactions are somewhat defensive, enabling cells to adapt and endure (Liu *et al.*, 2025a). However, homeostasis fails when stress exposure surpasses adaptive capacity, which can result in organelle failure, cellular damage, and even the activation of cell death pathways like necrosis or apoptosis (Chen *et al.*, 2025a).

Membrane dynamics and transport

The cell membrane is a dynamic structure that controls molecular exchange and signal transmission between the intracellular and extracellular environments in addition to acting as a physical barrier (Horn and Jaiswal, 2018). The membrane may carry out highly regulated selective tasks while retaining the structural flexibility required for several physiological processes because to the lipid bilayer's composition, which is filled with integral and peripheral proteins (Muller *et al.*, 2019).

Depending on the physicochemical characteristics of the substances being carried, molecules travel across the membrane by a variety of methods (Alam *et al.*, 2023). Small, nonpolar molecules like carbon dioxide and oxygen can move through the membrane along a concentration gradient through simple diffusion without the need for energy (Yang and Hinner, 2015). On the other hand, polar compounds and ions need membrane proteins to help them diffuse via certain channels or transporters (Li *et al.*, 2021). Although this method gives more selectivity and regulation, it is still reliant on the concentration gradient (Drew and Boudker, 2024).

Maintaining the ideal intracellular composition depends heavily on active transport, especially when molecules need to be transferred against an electrochemical gradient or concentration (Alam *et al.*, 2023). Ion pumps like Na^+/K^+ -ATPase mediate this activity, which needs energy, usually in the form of ATP (Contreras *et al.*, 2024). In addition to preserving ionic balance, these pumps' action helps create membrane potentials, which are necessary for excitable cells like neurons and muscle cells to function (Kay, 2017).

Cells use vesicular processes in addition to molecular transport pathways to transport big particles and macromolecules (Ortega *et al.*, 2022). Through the creation of membrane vesicles, endocytosis—which can take many different forms, including phagocytosis, pinocytosis, and receptor-mediated endocytosis—allows items from the extracellular environment to be internalized (Banushi *et al.*, 2023). On the other hand, by the fusion of vesicles with the plasma membrane, exocytosis contributes to the secretion of substances such as proteins, hormones, and neurotransmitters (Liang *et al.*, 2017). Because membrane systems are dynamic, both processes heavily rely on cytoskeleton rearrangement and membrane protein control (Trozzi and Kunkowska, 2024).

One important component that integrates these different transport methods is electrochemical gradients (Benyamin *et al.*, 2023). The direction and speed of ion transport are determined by these gradients, which are created by variations in the electrical charge and ion concentration on either side of the membrane (Hughes *et al.*, 2022). Electrochemical gradients are used not just in passive transport but also in secondary processes like secondary active transport, which uses the energy contained in ion gradients to propel other molecules (Beckstein and Naughton, 2022). Therefore, electrochemical gradients are a crucial source of potential energy for sustaining cellular activity (Funk and Monsees, 2006).

Cellular signaling pathways

A key mechanism that allows cells to receive, process, and react in unison to a variety of internal and external stimuli is the cellular signal transduction system (Li, 2005). This process is essential for controlling cell proliferation, differentiation, metabolism, and survival because it involves a number of molecular activities that translate extracellular signals into certain biological responses (Long *et al.*, 2025).

G protein-coupled receptors (GPCRs) mediate a crucial signal transduction pathway (Liu *et al.*, 2021). By activating heterotrimeric G proteins upon ligand binding, these receptors—the largest family of membrane proteins—start cellular reactions (Liu *et al.*, 2024a). GPCR activation causes GDP to be exchanged for GTP at the $G\alpha$ subunit, which in turn controls a number of downstream effectors, including phospholipase C and adenylyl cyclase (McCudden *et al.*, 2005). Second messengers such cyclic adenosine monophosphate (cAMP) and inositol trisphosphate (IP3) are produced as a result of this activation and serve to enhance and prolong intracellular signals (Martin *et al.*, 2005).

Receptor tyrosine kinases (RTKs) are essential for controlling cell growth and differentiation in addition to GPCRs (Lin, 2025). Tyrosine residues in the intracellular domain are autophosphorylated during ligand-induced receptor dimerization, which activates RTK (Maruyama, 2014). Docking sites for adaptor proteins that start different signaling pathways, including as rat sarcoma / mitogen-activated protein kinase (Ras/MAPK), phosphoinositide 3-kinase / protein kinase B (PI3K/Akt), and phospholipase C gamma (PLC γ), are created by this phosphorylation (Raj *et al.*, 2022). These pathways support cell cycle regulation, cellular metabolism, and gene expression regulation (Tomuleasa *et al.*, 2024). Oncogenesis is frequently linked to RTK dysregulation because of the unchecked activation of proliferative signals (Du and Lovly, 2018).

In order to amplify and spread signals throughout the cell, second messengers are essential mediators (Newton *et al.*, 2016). Signal conversion from the membrane to different cellular compartments is made possible by molecules including cAMP, Ca^{2+} , and diacylglycerol (DAG) (Tewson *et al.*, 2012). Rapid and reversible second messenger dynamics allow cells to adjust to changes in their surroundings (Su *et al.*, 2024). Certain enzymes, including as phosphodiesterases, protein kinases, and phosphatases, regulate the quantities of second messengers, guaranteeing the precision and timeliness of the signal (Seok, 2021).

A key component of cellular communication networks is signal integration, which involves the interaction of several signaling pathways to provide a coordinated response (Meduri, 2026). Instead of reacting to stimuli in a linear fashion, cells use interconnected signaling networks (Pawson and Scott, 2010). Cells are able to decipher complicated signal combinations through cross-talk between pathways, such as the convergence of MAPK pathways or the interaction between GPCRs and RTKs (Almela *et al.*, 2013). These processes guarantee that decisions made by cells, including proliferation, apoptosis, or differentiation, are founded on thorough information integration (Costa-Neto and Parreiras-E-Silva, 2025).

Energy metabolism

All cellular activity, including the conversion of nutrients into ATP, the biological energy currency, is primarily supported by energy metabolism (Liu *et al.*, 2025b). In addition to determining cell survival, sufficient energy supply controls a number of physiological functions, including biosynthesis, active transport, proliferation, and stress response (Fulda *et al.*, 2010).

Glycolysis, the breakdown of glucose in the cytoplasm into pyruvate by a sequence of enzyme processes, is the first step in energy metabolism (Chandel, 2021). This process produces nicotinamide adenine dinucleotide hydride (NADH), a high-energy electron carrier, and modest amounts of ATP directly through substrate-level phosphorylation (Kierans and Tay-

lor, 2024). Despite having a lower efficiency than oxidative processes, glycolysis has the benefit of producing energy quickly and can happen in both aerobic and anaerobic environments, making it a versatile metabolic pathway under a range of physiological circumstances (Soto-Herederó *et al.*, 2020).

After entering the mitochondria, the resultant pyruvate undergoes oxidative decarboxylation to produce acetyl-CoA, which subsequently enters the Krebs cycle (citric acid cycle) (Arnold and Finley, 2023). This cycle acts as a center for intermediate metabolism, generating vital precursors for the production of biomolecules in addition to NADH and flavin adenine dinucleotide (FADH $_2$) as electron donors (Williams and O'Neill, 2018). Therefore, the Krebs cycle contributes to both energy production and the integration of catabolic and anabolic processes inside cells (Franco and Serrano-Marín, 2022).

Oxidative phosphorylation, which occurs in the inner mitochondrial membrane, is the last and most effective step in the synthesis of ATP (Bonora *et al.*, 2012). The electron transport chain is involved in this process (Casanova *et al.*, 2023). It creates a proton gradient across the mitochondrial membrane by moving electrons from NADH and FADH $_2$ through a respiratory protein complex (Goldman *et al.*, 2023). ATP synthase then uses this electrochemical gradient to generate a lot of ATP (Althaher and Alwahsh, 2023). Because of its effectiveness, this mechanism serves as aerobic eukaryotic cells' main energy source (Litty and Müller, 2022).

Energy metabolism is essential for controlling cellular activity in addition to its fundamental role in ATP synthesis (Kurniawan *et al.*, 2025). Metabolic sensors like AMPK, which organizes adaptive responses to energy deficiencies by boosting catabolic processes and inhibiting anabolic pathways, keep an eye on the energy situation of cells (Khairullah *et al.*, 2026a). On the other hand, pathways like mechanistic target of rapamycin (mTOR) stimulate cell growth and proliferation when there is an abundance of energy and nutrients (Soliman, 2013). The dynamic balance between energy conservation and consumption is reflected in the interaction between AMPK and mTOR (Inoki *et al.*, 2012).

Numerous clinical disorders, such as cancer, diabetes, and neurodegenerative diseases, have been found to exhibit dysregulation of energy metabolism (Yuan *et al.*, 2024). Metabolic reprogramming may promote the growth and survival of aberrant cells, according to changes in metabolic preferences, such as elevated aerobic glycolysis in cancer cells (the Warburg effect) (Liberti and Locasale, 2016). Thus, a comprehensive grasp of energy metabolism is crucial for the development of metabolic-based treatment approaches as well as for basic physiology.

Cellular dysfunction as the basis of disease

Cellular dysfunction is the main basis underlying various pathological processes, when disturbances in the physiological mechanisms of cells cause failure of homeostasis and develop into diseases at the tissue and organ levels. The progression from cellular homeostatic failure to oxidative stress, mitochondrial dysfunction, abnormal signaling, and disease development is summarized in Figure 2.

Disruption of cellular homeostasis

Cellular homeostasis dysfunction, in which cells' inability to maintain internal balance results in compromised biochemical and structural functioning, is a crucial event that underlies a number of pathogenic pathways (Lemanowicz *et al.*, 2026). Long-term stress exposure or the incapacity of cellular regulatory mechanisms to adjust to drastic environmental changes are typically the causes of this illness (Fulda *et al.*, 2010).

Oxidative stress, which happens when the generation of reactive oxygen species (ROS) surpasses the capability of cellular antioxidant systems, is one significant type of homeostatic disruption (Martindah *et al.*, 2025). Superoxide, hydrogen peroxide, and hydroxyl radicals are examples of

ROS that can interact with lipids, proteins, and nucleic acids to cause extensive molecular damage (Li *et al.*, 2016). While protein oxidation can change the structure of enzymes and decrease their biological function, lipid peroxidation in cell membranes compromises the fluidity and structural integrity of membranes (Zheng *et al.*, 2024). Oxidative damage can cause mutations in deoxyribonucleic acid (DNA) that lead to neoplastic transformation (Maynard *et al.*, 2009). The main defense mechanisms are endogenous antioxidant systems, such as glutathione peroxidase, catalase, and superoxide dismutase (SOD), however under prolonged stress, their capacity may be exceeded (Poljsak *et al.*, 2013).

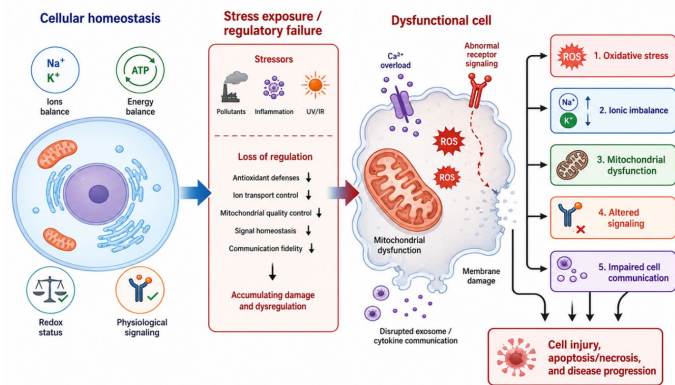


Figure 2. Cellular dysfunction pathways linking homeostatic failure to disease mechanisms.

Ionic imbalance is a major factor that disrupts cellular homeostasis in addition to oxidative stress (Qin *et al.*, 2026). Membrane potential, osmolarity, and enzymatic activity all depend on the regulation of ions like sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-) (Elliott and Cooper, 2024). Certain ions may accumulate or be depleted within the cell as a result of disruption of membrane channels or ion pump function (Bortner and Cidlowski, 2020). For instance, unchecked elevations in intracellular Ca^{2+} can activate phospholipases, endonucleases, and proteolytic enzymes, ultimately leading to cell death and structural damage (Khairullah *et al.*, 2026b).

The function of organelles, especially mitochondria, is also directly impacted by ionic imbalance (Osellame *et al.*, 2012). The electron transport chain can be disrupted by mitochondrial Ca^{2+} excess, which can also enhance the formation of ROS and cause the mitochondrial permeability transition pore (mPTP) to open, resulting in the loss of mitochondrial membrane potential and inability to produce ATP (Hurst *et al.*, 2017). This illness perpetuates the degenerative cycle of cellular destruction and energy failure (Zhang *et al.*, 2022).

Mitochondrial dysfunction

Reduced cell viability and the emergence of numerous diseases are directly caused by mitochondrial malfunction, a key mechanism in cellular physiological problems (Stańczyk *et al.*, 2024). In addition to being the main organelles that produce ATP, mitochondria are also hubs for metabolic signal integration, redox regulation, and the management of pathways leading to programmed cell death (Wang *et al.*, 2025).

Increased generation of ROS as a result of disruption of the electron transport chain (ETC) is a significant consequence of mitochondrial malfunction (Zhao *et al.*, 2019). Superoxide is produced as a result of incomplete oxygen reduction caused by electron leakage, especially in complexes I and III (de la Lastra *et al.*, 2026). When ROS production surpasses the capability of the cytosolic and mitochondrial antioxidant systems, oxidative stress builds up and damages respiratory proteins, membrane lipids, and mitochondrial DNA (mtDNA) (Liu and Chen, 2017). Under normal settings, ROS serve as regulated signaling molecules (Deepak *et al.*,

2026). Because damage to mtDNA interferes with the synthesis of ETC components, respiratory failure is exacerbated and a severe pathogenic feedback loop is created (Zhou *et al.*, 2021).

Depending on the extent and duration of damage, mitochondrial dysfunction is also strongly associated with the activation of cell death pathways, either through necrosis or apoptosis, in addition to redox disturbance (Khan *et al.*, 2022). Pro-apoptotic proteins like cytochrome c are released into the cytosol during apoptosis by mitochondrial outer membrane permeabilization (MOMP), which then activates caspases by forming the apoptosome (Zhou *et al.*, 2024). This procedure causes regulated and programmed cell death without causing a generalized inflammatory reaction (Rodríguez-González and Gutiérrez-Kobeh, 2023).

On the other hand, cells typically experience necrosis in cases of more severe mitochondrial damage, especially when there is a total failure of ATP generation (Nieminen, 2003). Energy depletion causes cell enlargement, plasma membrane rupture, and the release of intracellular contents into the extracellular environment by interfering with the maintenance of ionic homeostasis and membrane integrity (Guo *et al.*, 2024). A secondary inflammatory reaction frequently coexists with this illness, which may worsen tissue damage (Toba *et al.*, 2026).

Altered cell signaling

A major feature of the pathophysiology of many diseases is changes in cellular signaling pathways, which represent the inability of molecular communication systems to sustain appropriate physiological control (Lemanowicz *et al.*, 2026). Constitutive activation, pathological inhibition, or disarray of signaling networks can all lead to altered cell signaling, which eventually upsets the equilibrium between cell division, proliferation, and death (Duronio and Xiong, 2013).

Mutations in important receptor components or signal transduction proteins are frequently linked to aberrant activation of signaling pathways (Li *et al.*, 2024). For instance, excessive activation of downstream proteins like Ras or receptor tyrosine kinases (RTKs) might result in the transmission of proliferative signals that endure in the absence of external stimuli (Ledda and Paratcha, 2007). A key process in oncogenesis, this state causes cells to undergo a cycle of continuous division (Zhong *et al.*, 2025). Additionally, unchecked proliferative signals are amplified when tumor suppressor proteins or phosphatases are rendered inactive (Narla *et al.*, 2018).

On the other hand, blocking specific signaling pathways can also have serious negative effects (Lemmon *et al.*, 2016). Reduced activity of survival pathway signals, including PI3K/Akt, can make cells more susceptible to stress and cause excessive apoptosis (He *et al.*, 2022). This imbalance is frequently linked to tissue degeneration, especially in the nervous system, where a gradual decrease in neuron viability is caused by the loss of trophic signals (Roy *et al.*, 2023).

Another important component of altered cell signaling is dysregulation of the signaling network (Nair *et al.*, 2019). In order to guarantee integrated and contextual cellular responses, several signaling channels normally interact through cross-talk mechanisms (Vert and Chory, 2011). Pathological situations, on the other hand, cause this integration to be disrupted, which results in cells reacting to stimuli improperly or excessively (Papendorf *et al.*, 2022). For instance, an environment that encourages the continuous proliferation of aberrant cells can be created by concurrently activating proliferative pathways and inhibiting apoptotic processes (Kalimuthu and Se-Kwon, 2013).

Impaired cell communication

The coordination of biological processes at the tissue and organ system levels is made possible by intercellular communication (Ahmed and Xiang, 2011). In order to provide an integrated response to changes in the internal and external environment, this mechanism uses a variety of

chemical and physical mediators (Su *et al.*, 2024). When this communication mechanism is disrupted, physiological control becomes disorganized, which can lead to a number of medical disorders (Boaru *et al.*, 2025).

Disruption of paracrine and endocrine signaling, which is usually mediated by molecules like cytokines, hormones, and growth factors, is a significant type of cellular communication disruption (Su *et al.*, 2024). Target cells' sensitivity may be changed by imbalances in the synthesis or reaction to these mediators, leading to an excessive biological reaction (Tian *et al.*, 2025). When it comes to inflammation, for instance, excessive production of pro-inflammatory cytokines like interleukins and tumor necrosis factor can lead to a chronic inflammatory state that harms tissue, while reduced anti-inflammatory signaling might prevent inflammation from physiologically resolving (Chen *et al.*, 2017).

Exosomes have been found to be an essential part of vesicle-based intercellular communication in addition to soluble mediators (Maheshwari *et al.*, 2014). Exosomes are nanoscale extracellular vesicles that facilitate the targeted transfer of biological information between cells (Kalluri and LeBleu, 2020). They include proteins, lipids, ribonucleic acid (RNA), and other bioactive substances (Chen *et al.*, 2021). Exosomes are involved in immune response modulation, tissue homeostasis regulation, and regeneration under physiological settings (Lin *et al.*, 2020). However, the amount and makeup of exosomes can alter dramatically under pathological circumstances, sending signals that aid in the advancement of the disease (Isola and Chen, 2017). For instance, tumor cell-derived exosomes may include microRNAs or oncoproteins that encourage recipient cell angiogenesis, proliferation, and metastasis (Ahmadi and Rezaie, 2020).

Changes in receptor recognition processes or disturbances in signal internalization pathways can potentially lead to abnormalities in cellular communication (Nair *et al.*, 2019). Proper signal transmission can be hampered by mismatches between ligands and receptors as well as alterations in receptor expression on the cell surface (Held and Mariuzza, 2011). This ultimately jeopardizes the functional integrity of organs by causing a breakdown of coordination between cells within a tissue (Su *et al.*, 2021).

Cellular physiology in specific disease mechanisms

Cellular physiology plays a crucial role in explaining the underlying mechanisms of various diseases, where disruptions in cell function serve as the starting point for more complex pathological processes at the tissue and organ levels. Table 1 summarizes the major disturbances of cellular physiology in four major disease groups: cancer, metabolic disorders, neurodegenerative diseases, and infectious diseases.

Cancer

Loss of control over the processes of cell proliferation, differentiation, and death is a hallmark of cellular physiological abnormalities that culminate in cancer (Loftus *et al.*, 2022). Disruption of cell cycle regulation, which typically maintains the balance between proliferation and genomic checkpoint control, is the fundamental molecular cause of neoplastic transformation (Dash and El-Deiry, 2004).

Key elements including cyclins, cyclin-dependent kinases (CDKs), and CDK inhibitor proteins are typically altered in cell cycle dysregulation (Pellarin *et al.*, 2025). Without sufficient DNA repair, cells may be forced beyond crucial checkpoints, especially at the G1/S and G2/M phases, by excessive activation of the cyclin-CDK complex (Kaufmann, 1995). This illness increases the aggressiveness of cancer cells and encourages the gradual accumulation of genetic alterations (Bhat *et al.*, 2024). Additionally, the DNA damage surveillance mechanism is eliminated when tumor suppressor proteins like p53 and retinoblastoma (Rb) are inactivated, allowing cells with unstable genomes to proliferate (Chen *et al.*, 2020).

Resistance to apoptosis, or the inability of cells to undergo programmed cell death in spite of severe damage or stress signals that ought to cause cell elimination, is another crucial component of carcinogenesis (Mohammad *et al.*, 2015). Reduced caspase activation, disruption of both intrinsic and extrinsic apoptosis pathways, and an imbalance between pro-apoptotic and anti-apoptotic proteins in the Bcl-2 family are frequently linked to this resistance (Singh *et al.*, 2019). For instance, Bcl-2 overexpression can limit cytochrome c release and caspase cascade acti-

Table 1. Cellular physiology disturbances across specific disease mechanisms.

Disease group	Major cellular physiology disturbance	Key molecular mechanisms	Pathological consequences	References
Cancer	Loss of regulation of cell proliferation, differentiation, and apoptosis	Dysregulation of the cell cycle through abnormal cyclin-CDK activation; inactivation of tumor suppressors (p53, Rb); impaired DNA repair; apoptosis resistance mediated by altered Bcl-2 family signaling and reduced caspase activation; activation of PI3K/Akt and NF- κ B survival pathways	Uncontrolled cell proliferation, genomic instability, evasion of programmed cell death, tumor progression, and increased cancer aggressiveness	Loftus <i>et al.</i> (2022); Dash and El-Deiry (2004); Kaufmann (1995); Chen <i>et al.</i> (2020); Mohammad <i>et al.</i> (2015); Singh <i>et al.</i> (2019); Qian <i>et al.</i> (2022); Schiliro and Firestein (2021)
Metabolic disorders	Impaired cellular energy homeostasis and metabolic flexibility	Insulin resistance associated with disruption of IRS-PI3K/Akt signaling; reduced GLUT4 translocation; mitochondrial dysfunction; excessive ROS generation; activation of inflammatory pathways (IKK and JNK); intracellular lipid accumulation and lipotoxicity	Reduced glucose uptake, chronic hyperglycemia, impaired oxidative phosphorylation, sustained metabolic stress, and chronic inflammation	Clemente-Suárez <i>et al.</i> (2023a); Petersen and Shulman (2018); Huang <i>et al.</i> (2018); Khalid <i>et al.</i> (2021); Chandrasekaran and Weiskirchen (2024); Kowalczyk <i>et al.</i> (2021); Chen <i>et al.</i> (2025b)
Neurodegenerative diseases	Progressive neuronal dysfunction associated with impaired proteostasis and organelle dysfunction	Disturbance of Ca ²⁺ homeostasis; impaired axonal transport; mitochondrial dysfunction; protein misfolding and aggregation (β -amyloid, α -synuclein, huntingtin); proteasome dysfunction; unfolded protein response (UPR) activation; defective autophagy-lysosomal pathways; increased ROS production	Progressive neuronal loss, impaired synaptic transmission, neurotoxicity, cognitive decline, and motor dysfunction	Tesco and Lomoio (2022); Gao and Hong, 2008; Fricker <i>et al.</i> (2018); Cai and Tammineni (2017); Moreno-Gonzalez and Soto (2011); Ciechanover and Kwon (2017); Takalo <i>et al.</i> (2013); Kozlov <i>et al.</i> (2024)
Infectious diseases	Disruption of host cellular signaling and metabolic physiology by pathogens	Pathogen adhesion and receptor-mediated internalization; modulation of NF- κ B, MAPK, and PI3K/Akt signaling; inhibition of apoptosis; metabolic reprogramming (enhanced glycolysis and altered lipid metabolism); dysregulation of cytokine and exosome signaling	Enhanced pathogen survival and replication, immune evasion, chronic inflammation, tissue injury, and organ dysfunction	Thakur <i>et al.</i> (2019); Maginnis (2018); Xu <i>et al.</i> (2017); Song <i>et al.</i> (2024); Moreno-Altamirano <i>et al.</i> (2019); Alanazi <i>et al.</i> (2026); Troha and Ayres (2020); Marca <i>et al.</i> (2025)

vation by inhibiting mitochondrial membrane permeabilization (Qian *et al.*, 2022).

Additionally, cancer cells frequently display survival signals and metabolic changes that promote survival in demanding microenvironmental settings (Schiliro and Firestein, 2021). Increased proliferation, resistance to cell death, and the capacity to elude immunological responses are all facilitated by the activation of pathways like PI3K/Akt and nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) (Sadati *et al.*, 2025). An environment that promotes the clonal development of neoplastic cells is created when aberrant cell elimination mechanisms fail and unchecked proliferation occurs (Loftus *et al.*, 2022).

Metabolic disorders

A class of diseases known as metabolic disorders is defined by abnormalities in the control of cellular energy synthesis, storage, and utilization (Clemente-Suárez *et al.*, 2023a). An imbalance between the supply and demand of energy substrates results from these situations, which are caused by a breakdown of integration between important metabolic pathways and the signaling systems that regulate energy homeostasis (Liu *et al.*, 2025b).

Insulin resistance, a condition in which target cells like hepatocytes, adipocytes, and myocytes exhibit a reduced sensitivity to insulin despite elevated circulating levels of the hormone, is a key mechanism in metabolic diseases (Petersen and Shulman, 2018). Disruptions in the insulin receptor substrate (IRS) pathway and downstream signaling via PI3K/Akt are frequently linked to insulin resistance at the molecular level (Huang *et al.*, 2018). Insulin signal transduction can be inhibited by abnormal phosphorylation of IRS by serine/threonine kinases induced by inflammatory stress or excess lipids (Khalid *et al.*, 2021). This reduces the translocation of the glucose transporter (GLUT4) to the plasma membrane. As a result, cells absorb less glucose, which leads to chronic hyperglycemia (Chandrasekaran and Weiskirchen, 2024).

Cellular metabolic dysfunction includes altered metabolic flexibility, or the cell's capacity to alternate between using glucose, fatty acids, and other alternative substrates, in addition to defective insulin signaling (Petersen and Shulman, 2018). There is a greater dependence on inefficient fatty acid oxidation and a decrease in glucose consumption in pathological circumstances like obesity and type 2 diabetes mellitus (Ktenopoulos *et al.*, 2025). This imbalance is frequently accompanied by intracellular lipid buildup (lipotoxicity), which can impair the function of organelles like the endoplasmic reticulum and mitochondria (Nakamura, 2024).

By reducing oxidative phosphorylation capability and raising ROS generation, mitochondrial dysfunction is a major factor in the exacerbation of metabolic diseases (Kowalczyk *et al.*, 2021). In addition to harming cellular components, excessive ROS worsen insulin resistance by activating inflammatory pathways such inhibitor- κ B kinase (IKK) and c-Jun N-terminal kinase (JNK), which further increase the phosphorylation of inactive IRS (Chen *et al.*, 2025b). Chronic inflammation and metabolic stress interact to create a pathogenic loop that sustains long-term metabolic failure (Onyango, 2018).

Neurodegenerative diseases

A collection of chronic illnesses known as neurodegenerative diseases are marked by a progressive loss of neuronal structure and functional deterioration, which eventually compromises the integrity of brain circuits and impairs cognitive and motor abilities (Tesco and Lomoio, 2022). At the cellular level, these disorders are caused by persistent, mutually reinforcing deficiencies in organelle malfunction, proteostasis systems, and synaptic connectivity (Gao and Hong, 2008).

Neuronal dysfunction, which includes a reduction in neurons' capacity to sustain electrical excitability, synaptic transmission, and the structural integrity of axons and dendrites, is one of the fundamental causes

underpinning neurodegeneration (Fricker *et al.*, 2018). Ionic homeostasis disruptions, especially those involving Ca^{2+} , are important in this process because unchecked intracellular Ca^{2+} accumulation can trigger phospholipases and proteolytic enzymes that harm neuronal membranes and cytoskeletal integrity (Gu *et al.*, 2025). Moreover, the dispersion of mitochondria and synaptic vesicles is hindered by reduced axonal transport efficiency, which exacerbates the local energy deficit at the synaptic terminal and interferes with neurotransmitter transmission (Cai and Tammini, 2017).

Protein misfolding, a disorder in which proteins fail to attain their proper three-dimensional structure and subsequently gather in intracellular or extracellular aggregates, is another essential element (Moreno-Gonzalez and Soto, 2011). Through a number of pathways, such as compromised proteasome activity, unfolded protein response (UPR) activation, and disruption of synaptic function, these misfolded proteins can be hazardous (Wu and Lin, 2024). The build-up of certain proteins, including mutant β -amyloid, α -synuclein, and huntingtin, contributes to progressive neuronal dysfunction in disorders like Alzheimer's, Parkinson's, and Huntington's (Kim *et al.*, 2022a).

In order to prevent the build-up of aberrant proteins, cells have a protein quality control system that includes molecular chaperones, the ubiquitin-proteasome system, and the autophagy-lysosomal route (Ciechanover and Kwon, 2017). However, this system's capacity is frequently exceeded or its effectiveness declines in neurodegenerative illnesses, which leads to the ongoing build-up of protein aggregates and increased cellular stress (Takalo *et al.*, 2013). By producing more ROS, which hasten biomolecular damage, the combination of proteotoxic stress and mitochondrial dysfunction also impairs neural function (Kozlov *et al.*, 2024).

Infectious diseases

A dynamic interplay between pathogens and host cells, including adhesion, invasion, reproduction, and modification of biological responses, is reflected in infectious disorders (Thakur *et al.*, 2019). In addition to its inherent virulence, a pathogen must be able to take advantage of and alter host cells physiological processes in order to successfully start an infection (Pokorzynski and Groisman, 2023).

Tissue tropism and colonization efficiency are determined by a particular contact between a pathogen ligand and a host cell surface receptor, which typically starts the first stage of infection (Maginnis, 2018). Through direct cell membrane penetration or receptor-mediated endocytosis, this binding can initiate pathogen internalization (Xu *et al.*, 2017). Once within the cell, the virus avoids the majority of humoral immune response mechanisms and gains access to the nutrient-rich intracellular environment (Zhou *et al.*, 2025a).

Manipulating host cellular signaling pathways to establish favorable conditions for survival and reproduction is a crucial tactic used by viruses (Song *et al.*, 2024). Numerous bacteria and viruses can alter the inflammatory response, prevent apoptosis, or increase the survival of infected cells by interacting with pathways such NF- κ B, MAPK, and PI3K/Akt (Chisompola *et al.*, 2025). For instance, several viruses encode proteins that either imitate or block host signaling regulators, changing the ratio of pathogenic to protective responses (Moreno-Altamirano *et al.*, 2019).

In order to meet their energy needs, viruses can also take advantage of the host cell's metabolic system (Alanazi *et al.*, 2026). Metabolic reprogramming, such as enhanced glycolysis or modified lipid metabolism, which supplies substrate for pathogen replication, frequently coexists with these alterations (Liu *et al.*, 2024b). Prolonged metabolic changes brought on by persistent infections might occasionally result in tissue damage and organ malfunction (Troha and Ayres, 2020).

Another common tactic used by infections to avoid the immune system is disruption of cellular communication pathways, such as cytokine and exosome production (Marca *et al.*, 2025). Pathogens can either restrict immune cell activation or, on the other hand, cause an overactive in-

flammatory response that harms host tissue and promotes the spread of infection by modifying the production of inflammatory mediators (Chen *et al.*, 2017).

Therapeutic targets based on cellular physiology

Cellular physiology-based therapeutic targeting approaches have become an important strategy in the development of modern therapies that focus on correcting the underlying mechanisms of cell dysfunction. Table 2 summarizes cellular physiology-based therapeutic approaches that target fundamental mechanisms in the regulation of cell function. Cellular physiology-based therapeutic strategies and emerging technologies are conceptually summarized in Figure 3.

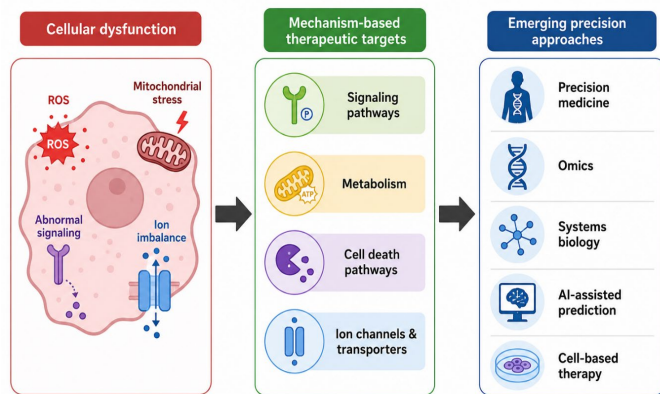


Figure 3. Cellular physiology-based therapeutic strategies and emerging technologies.

Targeting cell signaling pathways

A crucial therapeutic strategy in contemporary drug research is to target cellular signaling pathways, especially in conditions where the control of cell survival, proliferation, and differentiation is disrupted (Li *et al.*, 2025).

This strategy is predicated on the idea that important signal transduction components can be specifically altered to inhibit pathogenic activity or restore physiological balance without impairing overall cellular function (Du *et al.*, 2026).

Kinase inhibitors, which target phosphorylating enzymes including receptor tyrosine kinases (RTKs), serine/threonine kinases, and downstream elements of signaling cascades like MAPK and PI3K/Akt, are among the most popular strategies (Baldi *et al.*, 2025). By adding phosphate groups to target proteins, kinases modify their activity, location, or connections with other molecules, acting as key regulators of intracellular signal propagation (Ardito *et al.*, 2017). Excessive signal amplification, which is frequently present in diseases like cancer and other proliferative disorders, can be stopped or lessened by inhibiting kinase activity (Pellari *et al.*, 2025). Kinase inhibitors function mechanistically by either maintaining the target protein's inactive conformation or competing with ATP at the enzyme's active site, which lowers the effectiveness of pathogenic signal transmission (Smyth and Collins, 2009).

Receptor modulation, which attempts to control cells' initial reaction to external stimuli, is another crucial strategy (Su *et al.*, 2024). This tactic uses allosteric modulators, partial agonism, and receptor antagonism to change the sensitivity or specificity of receptors to their ligands (Wold and Zhou, 2018). It is possible to exert upstream regulatory control over a variety of downstream pathways by controlling signaling at its earliest stages through receptor activity modulation (Hengge-Aronis, 2002). Receptor modulation is frequently used in clinical settings for receptors related to neurotransmission, inflammation, and cell proliferation (Alves *et al.*, 2013).

Targeting signaling pathways has the primary benefit of enabling more focused interventions than traditional medicines due to their comparatively high degree of specificity for particular biological components (Marensi *et al.*, 2025). However, treatment resistance or compensating alternate routes can present difficulties due to the intricacy of cellular signaling networks, redundant mechanisms, and cross-talk between pathways (Volinsky and Kholodenko, 2013). Therefore, to increase the long-term efficacy of therapy, combinatorial techniques and systems-based

Table 2. Cellular physiology-based therapeutic targeting strategies in disease mechanisms.

Therapeutic target category	Primary target	Mechanism of action	Example interventions / approaches	Therapeutic implications	References
Targeting cell signaling pathways	Cell surface receptors, kinases, and intracellular signaling cascades (RTKs, MAPK, PI3K/Akt)	Modulation of signal transduction through kinase inhibition, receptor antagonism, partial agonism, or allosteric regulation to suppress pathogenic signaling and restore physiological balance	Kinase inhibitors; receptor antagonists; partial agonists; allosteric modulators; combinatorial signaling-targeted therapy	Selective control of cell survival, proliferation, and differentiation with improved therapeutic specificity; may reduce pathological signaling but can be limited by resistance and pathway cross-talk	Li <i>et al.</i> (2025); Du <i>et al.</i> (2026); Baldi <i>et al.</i> (2025); Ardito <i>et al.</i> (2017); Smyth and Collins (2009); Su <i>et al.</i> (2024); Wold and Zhou (2018); Volinsky and Kholodenko (2013); Mount <i>et al.</i> (2015)
Modulation of metabolism	Cellular bioenergetic pathways, metabolic sensors, and mitochondrial function	Reprogramming cellular energy utilization by regulating glycolysis, oxidative phosphorylation, substrate switching, and AMPK–mTOR signaling; restoration of redox and metabolic homeostasis	Metabolic-based therapies; glycolysis inhibition; AMPK activation; mTOR inhibition; mitochondrial-targeted interventions	Restoration of energy balance, reduction of abnormal proliferation, improved metabolic flexibility, decreased ROS production, and enhanced cellular adaptation	Imig (2022); Nesci (2022); Ma and Li (2015); Park <i>et al.</i> (2020); Liberti and Locasale (2016); Smith <i>et al.</i> (2018); Inoki <i>et al.</i> (2012); Garza-Lombó <i>et al.</i> (2018); Wang <i>et al.</i> (2025); Clemente-Suárez <i>et al.</i> (2023b)
Targeting cell death pathways	Apoptotic and necrotic regulatory pathways	Induction of programmed cell death via intrinsic and extrinsic apoptosis pathways or inhibition of uncontrolled necrosis to preserve tissue integrity	Apoptosis-inducing agents; mitochondrial membrane regulators; death receptor-targeted therapies; necrosis inhibitors; mitochondrial stabilizers	Elimination of abnormal cells, protection of healthy tissue, reduced inflammatory injury, and maintenance of tissue homeostasis	Hajibabaei <i>et al.</i> (2023); Mustafa <i>et al.</i> (2024); Yang <i>et al.</i> (2015); Elmore (2007); Di Meo <i>et al.</i> (2016); Arguello and Haisma (2021); Wong (2011); Loftus <i>et al.</i> (2022); Fink and Cookson (2005); Fulda <i>et al.</i> (2010)
Ion channels and transporters	Ion channels (Na ⁺ , K ⁺ , Ca ²⁺ , Cl ⁻) and membrane transporters (Na ⁺ /K ⁺ -ATPase, Ca ²⁺ -ATPase)	Regulation of ion movement, membrane potential, and electrolyte homeostasis using channel blockers, activators, and transporter modulation	Calcium channel modulators; sodium channel inhibitors; transporter-targeted agents; allosteric channel modulators	Rapid and targeted regulation of cellular excitability, secretion, contraction, and ionic homeostasis; applicable in cardiovascular, neurological, and metabolic disorders	Dubyak (2004); Subramanyam and Colecraft (2015); Tanner and Beeton (2018); Rahaman <i>et al.</i> (2026); Contreras <i>et al.</i> (2024); Hutchings <i>et al.</i> (2019); Rajakulendran and Hanna (2016); Dai and Khalil (2025); Gentile <i>et al.</i> (2025)

approaches are frequently required (Mount *et al.*, 2015).

Modulation of metabolism

In order to address the physiological dysfunctions that underlie a variety of diseases, metabolic modulation is a therapeutic approach that focuses on rearranging cellular bioenergetic and biosynthetic pathways (Imig, 2022). This method is predicated on the idea that cellular metabolism is extremely flexible and may be reprogrammed in response to disease states, environmental changes, and energy demands (Nesci, 2022).

Metabolic-based therapy, which focuses on important energy production and distribution routes such glycolysis, the citric acid cycle, and oxidative phosphorylation, is a significant type of metabolic intervention (Ma and Li, 2015). A change in metabolic preferences that promotes aberrant cell survival takes place in some pathological circumstances, such as cancer and chronic metabolic diseases (Park *et al.*, 2020). For instance, an increased dependence on aerobic glycolysis despite adequate oxygen availability is known as the Warburg effect (Liberti and Locasale, 2016). The goal of therapeutic therapies that target this route is to restore the cell's metabolic balance while blocking the energy source that promotes abnormal proliferation (Feitelson *et al.*, 2015).

Additionally, cellular energy reprogramming is becoming a more pertinent strategy when it comes to chronic inflammation and degenerative disorders (Alle *et al.*, 2021). In order to meet the physiological requirements of the cell, this process entails changing the direction of energy substrate usage, such as alternating between the oxidation of glucose, fatty acids, and glutamine (Smith *et al.*, 2018). AMPK and mTOR, two important energy sensors that operate as essential integrators between cell growth responses and nutritional status, can be modulated to regulate this regulation (Inoki *et al.*, 2012). For instance, mTOR suppression can restrict excessive anabolic activities and lower the cell's metabolic load, whereas AMPK activation encourages enhanced catabolism and energy efficiency (Garza-Lombó *et al.*, 2018).

Influencing mitochondrial activity, the site of energy synthesis, is another method of metabolic control (Wang *et al.*, 2025). In order to restore cellular energy homeostasis, it is crucial to improve oxidative phosphorylation efficiency, lower ROS production, and restore mitochondrial dynamics (fusion and fission) (Clemente-Suárez *et al.*, 2023b). These treatments affect signaling pathways that depend on the cell's redox and metabolic state in addition to ATP generation (Adebayo *et al.*, 2021).

Targeting cell death pathways

In many clinical diseases where there is an imbalance between cell survival and elimination, controlling cell death pathways is a crucial therapeutic approach (Hajibabaei *et al.*, 2023). In order to restore tissue homeostasis, this mechanism relies on controlling both programmed and non-programmed cell death processes, either by removing aberrant cells or shielding healthy cells (Mustafa *et al.*, 2024).

The controlled, non-inflammatory activation of pathways leading to programmed cell death, or induction of apoptosis, is one main strategy (Yang *et al.*, 2015). The intrinsic (mitochondrial) and extrinsic (death receptor) routes are the two primary ways that apoptosis can be started (Elmore, 2007). Intracellular stressors including oxidative stress, DNA damage, or mitochondrial failure set off the intrinsic route, which subsequently causes the permeabilization of the mitochondrial membrane and the release of cytochrome c into the cytosol (Di Meo *et al.*, 2016). Executor caspases, which are in charge of the targeted destruction of cellular components, are activated as a result (Nadendla *et al.*, 2025). In the meantime, ligand binding to surface receptors like Fas or the tumor necrosis factor (TNF) receptor activates the extrinsic pathway, which starts the caspase cascade by creating the death-inducing signaling complex (DISC) (Arguello and Haisma, 2021). In order to eradicate cancer cells or cells undergoing pathological change without causing an overwhelming

inflammatory reaction in the surrounding tissue, apoptosis induction is frequently utilized therapeutically (Wong, 2011).

On the other hand, necrosis inhibition is a crucial strategy when unchecked cell death results in significant tissue damage (Loftus *et al.*, 2022). Loss of plasma membrane integrity, cell enlargement, and the release of intracellular contents that sets off a subsequent inflammatory response are the hallmarks of necrosis (Fink and Cookson, 2005). Severe energy depletion, acute oxidative stress, or irreversible disturbance of ionic equilibrium are common causes of this process (Qin *et al.*, 2026). Necrosis inhibition is used therapeutically to preserve the integrity of cell membranes, stabilize mitochondrial function, and lessen the activation of inflammatory pathways brought on by damage-associated molecular patterns (DAMPs) produced from lysed cells (Qi *et al.*, 2025).

Since cell fate decisions are frequently influenced by the level of stress and energy availability, strategies aimed at cell death pathways also involve adjusting the ratio of necrosis to apoptosis (Fulda *et al.*, 2010). While extreme energy deficit encourages the shift to necrosis, conditions with adequate ATP often favor apoptosis (Galluzzi *et al.*, 2017). Therefore, a more regulated type of cell death may be indirectly directed by actions that preserve the cell's energy condition (Mustafa *et al.*, 2024).

Ion channels and transporters

By controlling ionic currents, membrane potential, and the distribution of electrolytes both inside and outside of cells, ion channels and membrane transporters play a crucial role in preserving cellular homeostasis (Dubyak, 2004). Numerous physiological functions, including as electrical excitability, muscular contraction, secretion, and signal transduction, depend on these protein structures (Kaura and Hopkins, 2024). These systems are important therapeutic targets in contemporary pharmacology because their dysfunction or dysregulation frequently contributes to the pathophysiology of numerous illnesses (Rahaman *et al.*, 2026).

Ion channels work by controlling and selectively permitting the passage of particular ions across cell membranes in response to electrochemical gradients (Subramanyam and Colecraft, 2015). Particularly in excitable tissues like neurons and cardiomyocytes, sodium, potassium, calcium, and chloride channels all have different functions in defining the physiological properties of cells (Tanner and Beeton, 2018). Excitability disorders, including cardiac arrhythmias, epilepsy, or neuromuscular problems, might result from changes in these channels' function (Ramos-Mondragon *et al.*, 2025). In order to address electrical dysfunction at the cellular level, ion channel activity modulation is a crucial strategy (Levitani, 1988).

Active membrane transporters, in addition to ion channels, are essential for preserving metabolic and ionic balance (Neverisky and Abbott, 2015). In order to move molecules against concentration gradients, transporters like Na⁺/K⁺-ATPase, Ca²⁺-ATPase, and other cotransporters and antiporters use energy from ATP or ion gradients (Contreras *et al.*, 2024). Abnormal intracellular ion buildup, osmolarity alterations, and organelle dysfunction—particularly mitochondria and the endoplasmic reticulum—can result from disruption of these processes (Sun *et al.*, 2025).

Blockers, activators, and allosteric modulators are pharmacological targets of ion channels that have been created for therapeutic purposes with the goal of controlling ion flow in accordance with physiological requirements (Hutchings *et al.*, 2019). For instance, calcium channel modulation can influence vascular smooth muscle contractility and lower blood pressure, while sodium channel inhibition is utilized to lessen neuronal hyperactivity in epilepsy (Rajakulendran and Hanna, 2016). This method enables the relatively quick and precise regulation of ion dynamics-dependent cellular processes (Dai and Khalil, 2025).

However, creating targeted treatments is difficult due to the intricacy of ion channel expression, which differs between tissues, and the presence of channel subtypes with similar activities (Gentile *et al.*, 2025). Additionally, the long-term efficacy of particular channel modification may

be diminished by cellular compensatory adaptations (Zhou *et al.*, 2025b). In order to improve specificity and clinical efficacy, ion channel-targeting treatment procedures are frequently coupled with other methods (Hutchings *et al.*, 2019).

Emerging approaches and technologies

The development of new approaches and technologies in cellular biology has opened up significant opportunities in understanding disease mechanisms and developing more precise and systems-based therapeutic strategies.

Precision medicine

A therapeutic strategy known as “precision medicine” focuses on customizing treatment plans according to each patient’s unique biological traits, such as genetic, epigenetic, proteomic, metabolomic, and cellular physiological dynamics (Marques *et al.*, 2024). By addressing biological variation between individuals and between cell groups within a single individual, this method represents a paradigm change from traditional “one-size-fits-all” therapy to more focused and adaptable approaches (Molla and Bitew, 2024).

Precision medicine at the cellular level is based on the knowledge that individual cells under diseased situations can show notable differences in metabolic status, signaling pathway activity, and gene expression (Gharipour *et al.*, 2022). Drug sensitivity, resistance mechanisms, and the cell’s ability to adjust to pharmacological stress are all impacted by this diversity in response to therapeutic treatments (Mansoori *et al.*, 2017). Determining the molecular profile of a cell is therefore essential for finding the most pertinent and successful treatment targets (Gordon *et al.*, 2018).

A thorough mapping of cellular physiological condition is made possible by the integration of multi-omics data (Liang *et al.*, 2022). While proteomics offers information on alterations in the expression and activity of functional proteins, genomic analysis can pinpoint the driving mutations that underlie disease transformation (Al-Amrani *et al.*, 2021). In contrast, metabolomics measures the metabolites involved in biosynthetic and bioenergetic pathways to reflect the true functioning status of cells (Petrova and Guler, 2025). This combination of methods enables the development of more precise biological system models to forecast therapy response (Johnson *et al.*, 2016).

Additionally, precision medicine makes use of developments in single-cell analysis technology, which enables the assessment of cellular heterogeneity at individual resolution (Lin *et al.*, 2024). This strategy is especially crucial for diseases like cancer, where different cell subpopulations within a single tumor may have unique genetic and functional traits that affect treatment response and possible resistance (Liu *et al.*, 2026). Therapies that target particular cell populations that contribute to the course of disease can be developed by comprehending this variety (Mount *et al.*, 2015).

Clinically, the use of precision medicine has improved treatment efficacy while lowering undesirable side effects by more precisely tailoring treatments (Krzyszczuk *et al.*, 2018). Additionally, this strategy increases the possibility of long-term success by creating combinatorial medicines that are customized to the patient’s molecular profile (Molla and Bitew, 2024).

Cell-based therapies

Cell-based therapies are therapeutic strategies that replace, repair, or alter the function of malfunctioning tissues by using living cells as interventional agents (Bashor *et al.*, 2022). This approach is predicated on the idea that cells can operate as active biological systems in reestablishing tissue homeostasis because of their innate ability to adapt, differentiate,

and interact with their milieu (Papamichail *et al.*, 2026).

Stem cell therapy, which makes use of stem cells with the capacity for multilineage differentiation and self-renewal, is a significant type of cell-based treatment (Deszcz, 2023). By developing into particular cell types in response to physiological demands, stem cells—whether embryonic, adult, or induced pluripotent stem cells (iPSCs)—can aid in tissue regeneration (Singh *et al.*, 2015). Stem cells not only directly aid in the replacement of injured cells but also have paracrine effects by secreting growth factors, cytokines, and extracellular vesicles that can speed up tissue repair, improve angiogenesis, and regulate the inflammatory response (Kim *et al.*, 2022b). The stem cells’ capacity to integrate into the tissue niche and preserve phenotypic stability following transplantation has a significant impact on the therapy’s efficacy (Jin *et al.*, 2023).

Immunotherapy is a cell-based strategy that aims to alter or improve the immune system’s capacity to identify and eradicate pathogenic cells, in addition to stem cell-based regeneration (Alali *et al.*, 2025). Anergy, fatigue, or a reduction in cytotoxic activity are common signs of immune cell failure in conditions like cancer and persistent infections (Rivera *et al.*, 2019). Increasing the specificity and efficacy of the immune response to pathogenic targets is the goal of therapeutic interventions like the use of activated T cells, chimeric antigen receptor T cells (CAR-T), or modified dendritic cells (Alnefaie *et al.*, 2022). More accurate antigen detection and a more potent effector response against aberrantly altered cells are made possible by these modified immune cells (Zhu *et al.*, 2026).

The interplay between therapeutic cells and local signals, such as inflammation, nutrition availability, and cytokine profiles, has a significant impact on the effectiveness of cell-based therapies at the microenvironmental level (Bhol *et al.*, 2024). The vitality, migration, or effector function of transplanted cells may be inhibited by an adverse environment (Baldari *et al.*, 2017). Therefore, to improve the effectiveness and durability of therapeutic effects, a variety of supplementary techniques are frequently employed, such as genetic engineering, cell preconditioning, or combination with pharmaceutical therapy (Liang and Du, 2021).

Omics and systems biology

Analytical frameworks for comprehending the structure and dynamics of biological systems at different levels of complexity, from molecular to network, are known as omics and systems biology techniques (Balagué *et al.*, 2022). This method highlights the fact that physiological and pathological occurrences are the outcome of nonlinear interactions between interrelated biological components within a dynamic regulatory network rather than being partially explained (Son *et al.*, 2020).

The study of an organism’s whole genetic makeup, including the detection of genetic variants including mutations, polymorphisms, and structural alterations that may impact gene expression and function, is known as genomics (Sinnott-Armstrong *et al.*, 2024). Mapping disease predisposing variables and identifying driver mutations that contribute to the onset and progression of pathological conditions are made possible by genomic data, especially in complex diseases like cancer and metabolic disorders (Johansson *et al.*, 2023).

Since proteins are the main effectors of biological function, proteomics expands the analysis to the protein level (Khalkhal *et al.*, 2019). Proteomic profiles more closely reflect the functional status of cells than genomic data alone because proteins are the result of gene expression and are subject to post-transcriptional and post-translational control (Ly *et al.*, 2014). Changes in protein expression, post-translational modifications, and protein-protein interactions that create signaling and metabolic networks are all part of this investigation (Zhang *et al.*, 2026).

In the meanwhile, metabolomics assesses the makeup of tiny metabolites, which are the end product of a cell’s biochemical activity (Wishart, 2019). A cell’s physiological state and adaptive response to environmental or pathological situations can be directly observed through changes in metabolic profiles (Metallo and Heiden, 2013). Metabolomics is thought

to be the closest approximation to the real biological phenotype since metabolites are so dynamic (Belhaj *et al.*, 2021).

Building more thorough models of biological systems is made possible by the integration of these three data layers inside a multi-level data integration framework (Gligorijević and Pržulj, 2015). This method creates biological interaction networks that represent causal and correlative interactions between cellular components by combining genomic, proteomic, and metabolomic data (Almasoud *et al.*, 2020). Therefore, systems biology focuses on comprehending the emergent features that result from intricate interactions within biological systems in addition to recognizing specific components (Díaz-Beltrán *et al.*, 2013).

In practical terms, the use of omics data has improved predictive powers in illness stratification, diagnosis, and the discovery of novel treatment targets (Chen *et al.*, 2023). Additionally, this method makes it possible to create computational models that mimic biological reactions to particular interventions, which helps with decision-making when creating mechanism-based treatments (Yetgin, 2025). The era of precision medicine and the creation of a new generation of treatment approaches that are more flexible and motivated by multidimensional data thus depend heavily on omics and systems biology (Tebani *et al.*, 2016).

Challenges and limitations

There are still some conceptual and technical challenges that affect the validity of translating fundamental research into clinical application in order to develop an understanding of cellular physiology as the foundation for disease causes and therapeutic targets. The primary obstacle is that biological systems are inherently complex, dynamic, interconnected, and non-linear, making it challenging to fully depict them using reductionistic methods (Aljuboori, 2021).

The intricacy of cellular systems, where several signaling routes, metabolic activities, and regulatory mechanisms interact in intricately linked networks, is one major drawback (Su *et al.*, 2024). It is not always possible to predict biological responses solely on a single pathway due to cross-talk, pathway redundancy, and positive and negative feedback loops (Vert and Chory, 2011). Because of this, it is challenging to find treatment targets that are truly specific without causing compensating effects from other pathways (Wang *et al.*, 2024).

Translating from in vitro to in vivo models is also fraught with difficulties. The physiological conditions of organisms, such as cell-cell interactions, the impact of the extracellular matrix, and the dynamics of the immune system and vascularization, are not fully replicated by cell culture systems, despite their great utility for the controlled study of molecular mechanisms (Pierre *et al.*, 2025). As a result, when applied to more complicated biological systems like animal or human models, the outcomes of in vitro investigations frequently exhibit notable discrepancies (Pun *et al.*, 2021).

Another important constraint on the advancement of cellular physiology-based methods is biological variability (Ilán, 2025). Different cellular reactions to the same stimulus or treatment can be caused by interindividual genetic variation, epigenetic variations, and environmental factors (Wattacheril *et al.*, 2023). Heterogeneity amongst cells within a tissue can produce subpopulations with unique physiological traits even within a single individual, making it more difficult to consistently anticipate therapeutic responses (Altschuler and Wu, 2010).

Moreover, a thorough comprehension of cell physiology in the setting of disease is similarly constrained by constraints in experimental models (Kay, 2017). While computational models rely on assumptions and parameters that have not been thoroughly confirmed scientifically, animal models frequently do not accurately reflect human physiology (Dupont and Gonze, 2024). These restrictions make it more difficult to precisely forecast clinical reactions and recreate entire biological systems (Frangogiannis, 2026).

Future perspectives

Numerous prospects for innovation in next-generation diagnostic and therapeutic techniques are presented by the development of cellular physiology studies as a foundation for disease processes and therapeutic targets (Long *et al.*, 2025). Future studies will increasingly focus on integrating transdisciplinary technologies that can more precisely and predictably capture the complexity of biological systems (Labusca, 2025).

The application of artificial intelligence (AI) to the study of cellular physiology is one such avenue (Zhang *et al.*, 2023). Large-scale biological data from cellular imaging, clinical data, and multiple omics platforms can be processed using this method to find hidden patterns that are challenging to find using traditional analysis (Sibilio *et al.*, 2025). Cellular behavior, such as stress reactions, signaling pathway activation, and sensitivity to therapeutic interventions, can be predicted using machine learning and deep learning models (Lazarou and Exarchos, 2024). AI thus functions as a computational tool that improves the understanding of extremely dynamic and complicated biological processes (Bhardwaj *et al.*, 2022).

Furthermore, one of the most important areas of current biomedical research is the discovery of therapeutic targets based on cellular principles (Qian *et al.*, 2024). This strategy focuses on the control of larger biological networks, such as connections between signaling pathways, metabolic regulation, and organelle dynamics, in addition to the inhibition or activation of a single particular molecule (Tu *et al.*, 2025). Finding important regulatory nodes within cellular networks is made possible by thorough mapping of biological systems, which is increasingly necessary for the identification of new targets (Galindez *et al.*, 2022). It is anticipated that this approach will improve therapy specificity while lowering the adverse consequences of excessively general interventions (Ripa *et al.*, 2025).

The creation of tailored medicines, which make use of each patient's unique molecular profile to create interventions that are most appropriate for their biological traits, also holds a lot of promise (Parekh *et al.*, 2023). In order to comprehend illness heterogeneity at the individual level, this method integrates genomic, proteomic, metabolomic, and single-cell analytic data (Evers *et al.*, 2019). Because different individuals react differently to the same treatment, a customized strategy maximizes clinical efficacy while reducing toxicity (Truong *et al.*, 2026).

Conclusion

Understanding the basic mechanisms that control both normal biological function and the course of disease is largely dependent on cellular physiology. It has been demonstrated that a number of pathological illnesses, including degenerative, metabolic, infectious, and malignant diseases, begin with dysfunction in basic processes like homeostasis, signal transduction, energy metabolism, and intercellular communication. Because biological processes are intricately interconnected, disruption of one element can set off a chain reaction that affects tissue and organ levels.

In addition to making disease pathophysiology more clear, an understanding of cellular physiology offers a logical foundation for locating more precise, mechanism-based treatment targets. The ability to thoroughly map cellular dysfunction is further improved by the integration of omics technology, systems biology, and molecular techniques. Therefore, cellular physiology is highly relevant as a basis for creating contemporary treatment approaches that are more accurate, flexible, and successful in dealing with the complexity of human disease.

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Conflict of interest

The authors have declared no conflict of interest.

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