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Cellular Symphonies: Exploring Organelle Dynamics In Immune Modulation And Cardiovascular Health

Swarup K. Chakrabarti[1*], Dhrubajyoti Chattopadhyay[1,2]

[1]H. P. Ghosh Research Center, HIDCO (II), EK Tower, New Town, Kolkata, West Bengal 700161, India.

[2]Sister Nivedita University, DG Block (Newtown), Action Area I, 1/2, New Town, West Bengal 700156, India.

[*]**Corresponding Author:** Swarup K. Chakrabarti, H. P. Ghosh Research Center, HIDCO (II), EK Tower, New Town, Kolkata, West Bengal 700161, India.

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Abstract

Organelles comprise intracellular membrane systems that enable them to form their own lipid bilayer-based enclosed compartments isolated from the cytoplasm. Numerous diseases, including chronic obstructive pulmonary disease (COPD), cardiovascular diseases (CVDs), infections, and neurodegenerative diseases (NDs), among others, include multiple organelle dysfunction at some point in their origin and evolution. As a result, maintaining the integrity of various organelles is essential to cell viability and function and may offer a therapeutic avenue for treating disorders affecting humans. Therefore, we provide an overview of organelles in this article, emphasizing their roles in the immunity regulation of human health and disease, particularly CVDs. We also offer a brief narrative discussion on the main mechanisms underlying the development of CVDs. Finally, we discuss how immune dysregulation resulting from organelle dysfunctions mediates the onset and progression of CVDs. We suggest that, because the endoplasmic reticulum, Golgi apparatus, mitochondria, lysosome, and ribosome are all interconnected, finding a shared, connected convergent immune signaling pathway—or pathways—that results in multiple organelle dysfunctions that underlie the genesis and progression of CVDs will make therapeutic efforts aimed at preserving the functionality of all organelles easier. It's anticipated that organelle-targeted approaches will keep drawing attention and grow to be a cornerstone of precision medicine in managing diseases affecting humans and significantly impacting public health.

Introduction

Types and functions of organelles in a human cell

Organelles comprise intracellular membrane systems, by which they create their enclosed compartments consisting of lipid bilayers, which are separated from the cytosol; the latter is also surrounded by the plasma membrane **[1,2]**. Organelles are classified into five broad types: endoplasmic reticulum (ER), Golgi apparatus, mitochondria, lysosome, and ribosome, each playing a distinct role in the cell **[3]**. Because the lipid bilayer of organelle membranes is impermeable to most of the hydrophobic molecules, the membrane of each organelle is equipped with membrane transport proteins, which are functionally engaged in importing and exporting specific metabolites. Additionally, each organelle membrane possesses mechanism(s) for importing specific proteins and incorporating them into the organelle as part of the structural organization, which makes a particular organelle unique from other types of organelles in terms of structure and function **[1]**.

Among five broadly classified organelles, ER is a large, continuous membrane-bound organelle comprised of functionally and structurally distinct domains and specific contact sites at the plasma membrane, mitochondria, Golgi apparatus, and endosomes that help ER to cross-talk with other organelles **[4]**. These distinct domains of ER are required for multiple cellular processes such as the synthesis of new proteins, their folding, and transport to other organelles, the formation of lipids, regulation of calcium levels, and exchange of macromolecules with other organelles at ER-membrane contact sites.

On the other hand, the Golgi apparatus is primarily responsible for processing and packaging molecules from ER, such as proteins, lipids, and carbohydrates, before being sent to other cellular compartments. As the Golgi apparatus is a significant site of carbohydrate synthesis, a large proportion of the carbohydrates that it makes are attached as oligosaccharide side chains to the many proteins and lipids that the ER sends to it before their transport through transport vesicles to other organelles, such as lysosomes. Importantly, recent studies suggest the Golgi apparatus plays a critical role as a signaling platform to integrate multiple innate immune pathways **[5]**.

Mitochondria are "powerhouses" of the cell and are responsible for generating energy in the form of ATP (adenosine triphosphate) through oxidative phosphorylation to perform critical functions of a cell **[6]**. Besides, the human mitochondrial genome confers coding information for 13 essential proteins, core constituents of the

mitochondrial respiratory complexes I–V embedded in the inner mitochondrial membrane. The electrochemical gradient generated by the complexes (I-IV) powers the terminal complex V of the respiratory chain; ATP synthase is an enzyme that catalyzes the synthesis of most cellular ATP **[7]**. Additionally, mitochondria produce metabolites for cell growth. The metabolites produced during the mitochondrial TCA (Tricarboxylic Acid) cycle, also known as the Krebs cycle, are carried into the cytosol, which is the building block for producing macromolecules **[8]**.

Lysosomes are organelles containing enzymes that break down proteins, lipids, and carbohydrates. Lysosomes dispose and recycle extracellular or intracellular macromolecules by fusing with endosomes, apart from serving as signaling nodes that sense and respond to changes in substrate metabolism to preserve critical cellular functions. Lastly, ribosomes are the sites of protein synthesis in the cell and are composed of two subunits, which can be either free in the cytoplasm or attached to the ER **[9,10]**.

Organelle Dysfunction Is Associated With A Wide Range Of Human Diseases.

The organelles' structural integrity and functional stability are required for cell viability and responsiveness. Multiple organelle dysfunction is critical in the pathogenesis and progression of many diseases, including chronic obstructive pulmonary disease, CVDs, infection, and NDs **[11-14]**. Therefore, the quality control of multiple organelles is critical to cell survival and function, and it may be a potential therapeutic target for human diseases. For example, organelle stress, such as ER stress, is associated with diabetes mellitus and obesity-associated disorders **[15,16]**. Also, ER dysfunction may play a causative role in a variety of neurological disorders such as cerebral ischemia, sleep apnea, Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), the prion diseases, etc. **[17-23]**. Additionally, mitochondrial disease prevalence has been estimated at 1 in 5000 worldwide **[24]**. Most mitochondrial pathologies that result in multisystemic disorders are believed to be caused by a failure to produce adequate ATP or energy. Though mitochondrial dysfunction (MD) can impact every organ in the body, clinical manifestations are more severe in high energy-demanding tissues like skeletal muscle cells, the central nervous system, and heart muscles **[25]**. Furthermore, as a secondary effect, MD causes immune dysregulation, which leads to autoimmune diseases **[26]**.

On the other hand, lysosomal storage diseases (LSD) are a family of disorders that arise from inherited gene mutations that perturb lysosomal homeostasis **[27]**. LSD is primarily caused by deficiencies in lysosomal enzymes and some non-enzymatic lysosomal proteins, resulting in abnormal macromolecular substrate storage. In addition to rare monogenic LSD, genes regulating lysosomal function have been linked to common sporadic NDs such as AD, PD, and ALS **[28]**. Also, aging lysosomes are associated with accelerated aging, age-related diseases, and decreased lifespan **[29]**.

Furthermore, ribosome biogenesis is a highly dynamic and coordinated process that involves the synthesis, modification, and assembly of ribosomal RNA (rRNA) with RP (ribosomal proteins) to form mature ribosomes **[30]**. Ribosome biogenesis and function defects are responsible for the pathogenesis of a diverse group of diseases known as ribosomopathies **[31]**. Ribosomopathies are diseases caused by mutations in RP or factors involved in RNA Pol I transcription and rRNA processing, which result in ribosome production or assembly disruption **[32]**. For instance, defects in ribosome synthesis have been linked to disease pathotypes in Treacher-Collins syndrome, Diamond-Blackfan anemia, and Shwachman-Diamond syndrome **[32]**.

A brief description of the primary mechanisms by which cardiovascular diseases arise.

Four disorders are generally referred to as "cardiovascular disease": aortic atherosclerosis, peripheral artery disease (PAD), cerebrovascular disease or stroke, and coronary artery disease (CAD), sometimes known as coronary heart disease (CHD). **[33]**. Among them, atherosclerosis is a pathologic process that can lead to disease in the arteries and aorta due to stenosis of the blood vessels, which results in reduced or no blood flow **[34]**. It is caused by complex interactions between lipoproteins, arterial vascular cells, and inflammatory cells. The key-initiating event in atherogenesis is the retention of apolipoprotein B-containing lipoproteins in the subendothelial space, followed by the recruitment of inflammatory monocytes and their differentiation into macrophages. Macrophages ingest lipoproteins to become lipid-loaded "foam cells," which, along with other immune cells and intimal smooth muscle cells, contribute to the progression of atherosclerotic lesions **[35]**. To elaborate, altered lipids stimulate inflammatory cells within the intima, producing chemokines and cytokines such as tumor necrosis factor (TNF-alpha), interleukin -1, -4, and -6, and interferon-gamma. These, in turn, stimulate additional leukocytes, endothelial cells, and adhesion molecules, particularly vascular cell adhesion molecule-1 (VCAM), intercellular adhesion molecule-1 (ICAM), and E-selectin, on the surface of the endothelium, among other mechanisms **[35,36]**. Interestingly, chronic activation of ER stress pathways promoting cell death is one cause of macrophage apoptosis in advanced atherosclerosis **[37]**.

Immune dysregulation: A central theme of organelle dysfunction leading to cardiovascular and other diseases.

Although organelles have distinct biochemical activities, an emerging concept has recently gained significant attention in regulating the innate and adaptive immune systems **[38,39]**. Thus, immune dysregulation associated with organelle dysfunction can lead to many diseases, including CVDs, affecting various body

organs. Likely, Immune dysregulation will further promote organelle dysfunction, together with exacerbation of severe disorders arising from dysfunctional organelles, establishing a vicious cycle of disease development and progression.

An Overview Of The Several Mechanisms By Which Organelles Regulate The Immune System.

The innate immune system is the first line of defense against microbial infection by distinguishing between self and non-self-components. The natural immune system primarily relies on the host pattern-recognition receptors (PRRs) expressed by innate immune cells such as macrophages and dendritic cells (DCs) to rapidly recognize and respond to signals derived from invading pathogens or injured self-cells that are targeted for destruction **[40,41]**. PRRs such as Toll-like receptors (TLRs), retinoic acid-inducible gene I (RIG-I)-like receptors (RLRs), and nucleotide-binding domain and leucine-rich repeat-containing molecules (NLRs) mediate the initial recognition of highly conserved structural motifs like pathogen-associated molecular patterns (PAMPs) **[42]**. This recognition initiates a series of signaling cascades that culminate in the activation of transcription factors such as nuclear factor-kB (NF-kB), interferon regulatory factor (IRF), and activator protein-1 (AP-1) that induce numerous downstream genes encoding a wide range of proteins **[40-42]**.

Importantly, organellar membranes not only define the intraorganellar space and maintain organelle identity but also serve as platforms for organizing regulatory complexes involved in innate immunity. For example, it is observed that components of the regulatory complex, which controls the activity of the proinflammatory transcription factor NF-kB, interact with the protein metadherin, a type-two transmembrane protein, at the cytosolic face of the ER, and this interaction is necessary for efficient activation of NF-kB in immune cells like B and T cells in response to cytokines or antigen receptor stimulation **[43]**. Furthermore, DCs serve as the link between innate and adaptive immunity. DCs can cross-present antigens to CD8+ and CD4+ T cells, activating them and triggering antigen-specific immune responses. DCs, like other innate cells, are myeloid in origin and are started by DAMPs (damage-associated molecular patterns) and PAMPs by expressing PRRs **[44,45]**. Importantly, ER regulates the effective antigen presentation of DCs, providing critical TLR (toll-like receptor) signaling through PAMPs, present in the pathogens, to contribute to the host's innate immune system **[46]**. Another example of the role of organelles in innate immunity comes from the Golgi apparatus, which serves as a signaling platform for innate immunity. The dispersion of the Golgi is essential for activating the NLRP3 inflammasome, and the interface between the Golgi, ER, and mitochondria is a critical hub in NLRP3 inflammasome activation **[47,48]**.

It is critical to investigate each organelle independently and their interactions with other organelles to understand how each one contributes to an individual's general immunity and the dysregulation associated with diseases such as CVD. Furthermore, the fundamental mechanisms of organelle-induced immunological dysregulation and other pathogenic processes may facilitate the development of therapies for diseases stemming from these remarkably immune mechanisms.

The role of Endoplasmic reticulum in immune regulation

ER is a critical organelle for protein synthesis, folding, modification, etc. **[49]** Unfolded proteins build up in the ER lumen when ER functions are compromised, triggering the unfolded protein response (UPR), which restores ER homeostasis. Under normal circumstances, the UPR restores ER homeostasis by attenuating protein synthesis or inducing the expression of various genes encoding molecular chaperones and protein processing enzymes that promote protein folding and post-translational modifications. The UPR is mediated by three distinct downstream signaling pathways such as IRE1 (inositol-requiring enzyme 1), PERK (protein kinase R (PKR)-like endoplasmic reticulum kinase), and ATF6 (activating transcription factor 6) that promote cell survival or apoptosis depending on the stressor, the intensity and duration of ER stress, and the cell type **[50]**. Direct links between ER stress and immune responses are also evident, but the mechanisms by which the UPR signaling cascade connects with immunity are complex, necessitating further foundational research to establish a solid link between ER and immune responses. That being said, many recent studies suggest immune roles of the UPR via direct cross-talk between ER stress-induced signaling pathways and immune responses. For example, ER stress is linked to autoimmune and inflammatory diseases such as diabetes, atherosclerosis, myositis, and inflammatory bowel disease, indicating a crucial role of ER stress in both innate and adaptive immune responses **[51,52]**. The UPR is also essential in physiological processes like developing immune cells, e.g., plasma cells, DCs, and eosinophils. Many recent studies of resistant cell types show that ER stress is central to immune processes such as differentiation, immune activation, and cytokine expression. Thus, targeting ER stress and the UPR with small molecules is emerging as a promising therapy for treating various diseases with underlying immune dysregulation, such as neurodegeneration, cancer, metabolic disorders, stroke, and heart disease **[53]**.

The Golgi apparatus is an emerging platform for innate immune functions.

Apart from the well-documented role of the Golgi apparatus in the activation of NLRP3 (nucleotide-binding domain, leucine-rich–containing family, pyrin domain–containing-3) inflammasome, a critical mediator of innate immunity, the membranous networks that connect the Golgi to the ER, mitochondria, endosomes (a type of intracellular sorting organelle), and autophagosomes (take up

damaged molecules or organelles and carry this cargo to the lysosomes) provide easy access to innate immune signal transduction and subsequent effector responses. Besides, the Golgi plays an essential role in modifying and transporting innate immune receptors, adaptors, and products as the sorting organelle. Several inflammatory cytokines, such as IL-6 and IFN-γ, are secreted via the ER-Golgi pathway **[54-56]**.

Mitochondria regulate immune responses.

The ability of mitochondria to regulate immune cell activation, differentiation, and survival constitutes its essential functions. The accumulating research over the years suggests that mitochondria can regulate immunity in multiple ways. Alterations in metabolic pathways (TCA cycle, oxidative phosphorylation) and mitochondria-induced transcriptional changes can result in different outcomes in immune cells **[57]**. For example, M1 macrophages typically possess a disrupted TCA cycle, which imparts the proinflammatory nature of M1 macrophages **[58]**. In contrast, M2 macrophages undergo ß-oxidation, resulting in anti-inflammatory responses. Besides, mitochondrial machinery such as metabolic pathways, amino acid metabolism, antioxidant systems, mitochondrial dynamics, mtDNA (mitochondrial DNA), mitophagy- a mitochondrial quality control mechanism enabling the degradation of damaged and superfluous mitochondria- and mtROS (mitochondrial reactive oxygen species) all play essential roles in immune function **[59]**. Importantly, NLRP3 inflammasome activation is also imparted by the mitochondrial components **[60]**. Also, mitochondrial dynamics play a prominent role in immune cell metabolism.

For example, mitochondrial fission and fusion regulate mitochondrial mass **[61]**. Nutrient deprivation increases mitochondrial fusion while suppressing mitophagy **[62]**. Prolonged DNA damage, on the other hand, results in mitochondrial fission **[63]**. More importantly, recent evidence suggests a role of mitochondrial dynamics in the activation of inflammasome. Induction of mitochondrial fission attenuates NLRP3 inflammasomal assembly and activation 64. In addition, mitochondrial signaling controls adaptive immunity, as evidenced by the regulation of T-cell activation by mitochondrial ROS. Additionally, pharmacologic inhibition of mitochondrial oxidative phosphorylation in vitro reduces T cell proliferation, implying that mitochondrial metabolism promotes T cell proliferation **[65]**.

The role of lysosomes in immunity

Emerging evidence suggests a critical role of lysosomes and lysosome-related organelles in innate immunity, mediated partly by sensing and responding to pathogen products, as evidenced by endolysosomal processing of TLRs and their ligands **[66]**. Also, while TLRs are primarily involved in innate immunity at the cell surface, there are several PAMP sensors in the cytosol, such as NOD-like receptors (NLRs), which recognize peptidoglycan motifs from bacterial cell walls and the RNA helicases RIG-I which identify viral double-stranded (dsRNA) and other distinct RNA species **[67]**. Some ligands for NLRs or RLRs (retinoic acid-inducible gene-I-like receptors) bind to these receptors via endolysosome cytosol transport mechanisms **[68]**. In addition, lysosomal proteases play pivotal roles in adaptive immunity regarding MHC presentation, among others.

The potential role of ribosomes in immune regulation

Recently, researchers have begun investigating ribosomes' potential role in innate immunity. However, it has long been known that virus-induced ribosome biogenesis is presumed to benefit infection by ensuring ribosome sufficiency for protein synthesis **[69]**. It is unclear whether the ribosome or the process of ribosome biogenesis can be subverted by viruses or incorporated into the cellular repertoire of innate immune responses. A recent study suggests that the ribosome is essential in conferring innate immunity to protect the host from viral infection and invasion. Interfering with rRNA accumulation by HCMV or dsDNA (double-stranded DNA) has caused the downregulation of High Mobility Group Box 2 (HMGB2). This chromatin-associated protein facilitates cytoplasmic (ds) DNA-sensing by cGAS (Cyclic GMP-AMP synthase), together with impairment of interferon beta (IFNB1) mRNA expression, which encodes a critical anti-proliferative, proinflammatory cytokine, in response to HCMV or dsDNA in uninfected cells **[69]**. This demonstrates that rRNA accumulation controls HMGB2 abundance and thus regulates innate immune responses to dsDNA.

The interconnectedness of endoplasmic reticulum, Golgi apparatus, mitochondria, lysosome, and ribosome in immune regulation

The membrane-bound organelles comprise eukaryotic cells that communicate with one another via vesicular trafficking pathways and membrane contact sites (MCSs), which play multiple roles in the exchange of metabolites, lipids, and proteins. Also, organelle interactions at MCSs are important for organelle division and biogenesis **[70]**. However, it is largely unknown whether immune regulation can be mediated in an orchestrated manner by many of the organelles in a human cell surrounded by a plasma membrane. Given that MCSs serve as interfaces for ion, lipid, and protein exchange, MCSs could also serve as platforms for assembly sites for protein complexes involved in immune cell signaling **[71]**.

The Inter-Organelle Interactions Regulating The Replicative Aging Process In Lower Eukaryotes, Such As

S. cerevisiae cells have been established **[72]**. Considering the immune dysregulation associated with the aging cycle, it is tempting to speculate that similar immune dysregulation could occur in higher eukaryotes in CVDs, orchestrated by the different membrane-bound organelles **[73,74]**. Identifying a common, interconnected signaling pathway or pathways that lead to multiple organelle dysfunctions by immunological dysregulation, which underpins the genesis and

progression of a wide range of human diseases, will facilitate therapeutic efforts aimed at maintaining the functionality of all organelles by focusing on a single, unifying pathway rather than several pathways that originate from each organelle. This possible notion has to be investigated further.

A succinct explanation of the immunological dysregulation associated with organelle dysfunction and cardiovascular diseases.

ER stress has long been known as a significant cause of CVDs **[75]**. Convincing evidence that ER stress occurred in atherosclerotic plaques, especially in the latter phases, has been shown by human atherosclerotic lesions and animal models of atherosclerosis **[76]**. More importantly, inflammatory signaling pathways are implicated in several stages of the development of atherosclerosis, a chronic inflammatory disease **[77]**. A growing body of evidence indicates that ER stress is linked to inflammatory signaling pathways via several mechanisms and contributes significantly to atherosclerotic CVDs by inducing immunological dysregulation. More specifically, in acute cellular ER stress conditions, the three ER stress sensors—PERK, IRE1, and ATF6—can trigger robust inflammatory responses via the UPR, especially in macrophages and endothelial cells **[78]**. Chronic ER stress usually increases intracellular ROS (reactive oxygen species) production, which can even reach toxic levels **[79]**. This is partially due to increased calcium release, increasing mitochondrial ROS production **[80]**. There is a link between oxidative stress and ER stress because elevated ROS causes accelerated ER dysfunction and directly affects protein secretion, folding, and degradation **[81]**. NLRP3 is activated by oxidative stress, which in turn triggers the NF-κB pathway and proinflammatory reactions **[82]**.

Furthermore, the development of ischemic cardiomyopathy, including myocardial infarction and ischemia/reperfusion (I/R) injury, is mediated by ER stress **[83]**. I/R injury has been connected to cellular damage and contractile failure, which can exacerbate CVDs by dysregulating immune responses **[84]**. This is partially caused by the JNK and p38 MAPK pathways being activated. Additionally, there is a growing body of evidence linking ER stress to cardiac hypertrophy and hypertension **[85]**. It is observed that pressure overload brought on by transverse aortic constriction (TAC) in cardiac hypertrophy results in prolonged ER stress **[86,87]**. This, in turn, led to the upregulation of ER stress chaperones, including GRP78, p-PERK, p-elF2α, CHOP, caspase 12, and p-JNK, the latter of which is a potent inducer of proinflammatory cytokines, and consequently, in hypertrophy-related cardiac myocyte apoptosis **[88]**.

CVDs, including heart failure, dilated cardiomyopathy, arrhythmia, and chronic atrial fibrillation, have structural changes and functional disorders of the Golgi apparatus **[89]**. Golgi acidity is critical for preserving the morphology of the Golgi and transporting various types of cargo. Cutis laxa is clinically associated with dysfunction of the Golgi-localized V-ATPase, which primarily regulates the Golgi luminal pH, caused by mutations in the ATP6VOA2 gene **[90]**. Neutrophils, monocytes, and innate immune cells usually migrate to the injury site when the heart is damaged or under stress. They produce mediators like ROS and proteases to eliminate the substances that cause heart damage **[91]**. In addition, cardiomyocytes typically release proinflammatory cytokines following injury, which might exacerbate the inflammatory response. According to recent studies, several inflammatory pathways are involved in myocardial inflammation **[92]**. These include the TNF/NF-κβ pathway, which is linked to cardiac infection and injury; pattern recognition receptors expressed by macrophages, such as Toll-like receptors (TLRs); and the oxidative and stress-activated caspase-1 inflammasome pathway and NLRP3, which lead to the pathogenesis and progression of cardiomyopathy **[93]**. Since the Golgi apparatus functions as a signaling platform to integrate the innate immune response, particular changes to its function that sense the natural component of immunity may result in CVDs like cardiomyopathy **[93]**.

To make matters worse, the I/R heart is the site of the vicious cycle of mtDNA-induced sterile inflammation and mitochondrial dysfunction—just one of the many routes that contribute to dysfunctional mitochondria-induced CVDs **[95]**. This is especially significant in the context of immunological dysregulation linked to CVDs. Furthermore, an ongoing accumulation of I/R damage and CM necrosis is caused by the accumulation of mutant mtDNA caused by excessive release of ROS from the mitochondrial permeability transition pore (MPTP). This accumulation of mtDNA also triggers a series of sterile inflammatory reactions linked to the recognition by inflammatory signaling receptors of intracellular contents released from necrotic and damaged cells (also known as damage-associated molecular patterns) and the recruitment of immune cells **[96]**.

Additionally, lysosomal dysfunction and its impact on immune regulation in CVDs are emerging research areas. Lysosomes play a crucial role in cellular homeostasis by digesting and recycling cellular waste. When lysosomal function is compromised, it can accumulate undigested material within cells, triggering a cascade of events that may contribute to immune dysregulation in CVDs. Furthermore, lysosomal dysfunction has been linked to atherosclerosis, which causes inflammation in the walls of the vessels **[97]**. Additionally, through a dysregulated immunological response, lysosomal dysfunction affects other CVDs, such as heart failure and myocardial infarction **[98]**. For instance, LSD is a prominent category of lysosome malfunction that is linked to CVDs. Hypertrophic and dilated cardiomyopathy are two of the many severe cardiac characteristics that many LSD patients exhibit **[99]**. Also, the fact that transcription factors like Transcription Factor EB (TFEB) are master regulators of the genes involved in lysosome formation and autophagy serves as additional evidence of the critical

function lysosomes play in CVDs **[100]**. In a mouse model, atheroprotection results from TFEB overexpression specific to macrophages **[101]**. Finally, several studies have demonstrated that ribosome dysfunction is a causative factor for several CVDs, including cardiac hypertrophy **[102]**.

Nevertheless, the molecular processes of cardiac hypertrophy remain unknown at this time. However, according to new research, ribosome biogenesis either promotes or inhibits the pathogenic process that leads to heart hypertrophy. Furthermore, ribosomal proteins L9 (RPL9) and L26 (RPL26) have been shown to express at lower levels in MI patients than in controls, according to recent bioinformatics research **[102]**. Consequently, RPL9 and RPL26 may be valuable targets for MI diagnosis or treatment **[103]**. Interestingly, another ribosomal protein, RPL13, blocks the translation of inflammatory genes, including CCL22, CXCL13a, and CCR3, to prevent inflammation and atherosclerosis brought on by macrophages **[104]**.

Conclusion & Future Directions:

In conclusion, given the critical roles that organelles play in a variety of physiological processes about cell development, maturation, and maintenance as well as immune system regulation, which helps to mitigate many human diseases such as cardiovascular diseases (CVDs) with underlying immune dysregulation, it is plausible that maintaining organelle health through pharmacological and dietary interventions will prevent the development of many diseases associated with organelle dysfunction, or at least slow it down. The capacity of next-generation organelle-targeted therapeutic medicines to accurately target particular molecular targets is making them a preferred choice for treatment. It is anticipated that techniques focused on organelles will draw more attention and establish themselves as a cornerstone of precision medicine in managing human ailments with significant ramifications for public health. On the other hand, from a fundamental perspective, exploring the complex link between immunological dysregulation and organelles opens up new avenues for cardiovascular research. By concentrating on pathways specific to different organelles, novel therapeutic approaches may be developed to reduce the chronic inflammation linked to CVDs, leading to more potent treatments. The potential to address immunological dysfunctions in CVDs using a precision medicine approach is becoming increasingly promising as we learn more about the cellular underpinnings.

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