IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

Review

A Narrative Review on the FSTL-1 Protein and its Current Known Impact on Cardiovascular Ischaemic Disease

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Abstract

This narrative review investigates the potential therapeutic role of FSTL-1 in addressing severe cardiac issues following myocardial infarctions (MI). Despite advances in modern medicine, MI persist as a leading global cause of death, with stem cell therapy falling short of expectations since the early 2000s. In contrast, FSTL-1, an emerging bone morphogenetic protein, demonstrates promise based on successful studies. We conducted a qualitative narrative synthesis of studies published in PubMed, Scopus, and Web of Science between January 2000 and May 2022. This research explores the intricate scientific aspects of FSTL-1's contribution to myocardial regeneration, utilizing a chronological approach to trace its progression from biological pathways to broader scenarios. It examines the mechanisms regulated by FSTL-1 and its effects on cardiac tissue and cells, highlighting its potential as a therapeutic agent emphasizing its multifaceted role in cardiac regeneration. By deepening our comprehension of FSTL-1, this study significantly contributes to knowledge advancement, offering insights into its role in addressing severe cardiac issues post-MI. By consolidating current knowledge and proposing new avenues for investigation, this work offers valuable insights into FSTL-1's significance in advancing cardiovascular health and post-MI recovery.

Introduction

In 54 countries belonging to the European Cardiology Society, there were 19.9 million new cases of cardiovascular disease (CVD) and 108.6 million individuals were found to be suffering from CVD in 2017. Ischaemic heart disease (IHD) is identified as the foremost expression of CVD, with 3.6 million new cases and 34.9 million individuals living with IHD.[1] CVD remains acknowledged as the leading cause of mortality in Europe, accounting for 4.1 million deaths annually, representing 47% of all deaths among women and 39% among men.[1]

Cardiac regenerative therapies have made significant progress over recent decades, aiming to address the limitations of traditional treatments for myocardial infarction (MI) and heart failure. Stem cell therapy has been a central focus, with various types, including embryonic, induced pluripotent, and mesenchymal stem cells, explored for their potential to replace damaged heart cells. However, challenges such as low engraftment rates, limited functional integration, and the risk of tumorigenicity have hindered widespread clinical success.[2] Cell-free therapies, such as the use of exosomes, microRNAs, and growth factors, have emerged as alternatives, targeting cardiac repair through cell signalling pathways. Tissue engineering approaches, including cardiac patches and 3D bioprinting, aim to create supportive environments for myocardial regeneration.[3] Gene therapy, utilizing techniques like viral vectors and CRISPR/Cas9, offers another avenue for promoting heart tissue repair by targeting specific pathways.[4] Biomaterials, such as injectable hydrogels and scaffolds, provide structural support and enhance cell survival, though challenges like immune response, vascularization, and functional integration persist.[5]

Despite these advancements, the field faces ongoing hurdles that require further research and innovation. Managing immune responses, ensuring adequate blood supply to regenerated tissues, and achieving long-term efficacy and safety in humans are critical areas of focus. Emerging approaches, including the investigation of novel biomolecules like FSTL-1 and immunomodulation strategies, offer promising new directions. The ultimate goal is to develop therapies that can reliably regenerate heart tissue, restore function, and improve outcomes for patients with heart disease. While significant strides have been made, translating these innovations into widely available clinical treatments remains a complex and ongoing challenge.

This dual focus on both cell-based cardiac regeneration techniques and the potential role of FSTL-1 underscores the urgency and significance of ongoing research endeavors in addressing the formidable burden of cardiovascular disease, particularly ischemic heart disease, in contemporary healthcare

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Editor: Francisco J. Bonilla-Escobar
Student Editors:Himal Karki & Sayan Sarkar
Proofreader: Amy Phelan
Layout Editor: Julian A. Zapata-Rios

Submission: Sep 19, 2023
Revisions: Dec 6, 2023, Jul 8, 2024
Responses: Mar 5, 2024, Agu 29, 2024
Acceptance: Oct 25, 2024
Publication: Dec 30, 2024
Process: Peer-reviewed

landscapes. The proposed objective of this narrative review is to comprehensively explore the role of FSTL-1 in cardiac regeneration, particularly within the context of ischemic heart disease. The review aims to synthesize current findings on FSTL-1's mechanisms of action, its therapeutic potential in promoting cardiac repair, and the challenges and opportunities for translating these insights into clinical practice. By integrating insights from basic research, preclinical studies, and emerging clinical evidence, the review seeks to provide a nuanced understanding of how FSTL-1 could be harnessed to improve outcomes for patients with ischemic heart disease.

Ischaemic Heart Disease

As mentioned before, Ischaemic Heart Disease (IHD) has been shown to be a severe pathology with a high mortality rate. Within a simplistic approach, IHD is caused by the acute occlusion of one or multiple sizable epicardial coronary arteries for more than 20 minutes, which can lead to an acute MI.[7] Typically, necrosis spreads from the sub-endocardium to the sub-epicardium region. Depending on the territory affected by the infarction, cardiac function is typically compromised, and current treatment options are limited. Due to the minor renewal capacity of the myocardium,[8] the infarcted area heals by scar formation, and often, the heart is remodeled, characterized by dilation, segmental hypertrophy of remaining viable tissue, and cardiac dysfunction.

The initial effects of oxygen deprivation will disrupt the sarcolemma arrangement in heart muscle tissue and relaxation of myofibrils, shortly followed by alterations in mitochondrial ultrastructure. These changes will then lead to mitochondrial dysregulation, affecting energy availability. More advanced stages of prolonged ischaemia will result in liquefactive necrosis of heart tissue, especially in the myocardium. The deposition of collagen type I and type III in fibrosis is essential in the short term to stop the rupture of ventricular walls; however, this mechanism makes it increasingly difficult for the injured to maintain its functional capacity. This is due to its ill effects on the ventricle's geometry, resulting in an accentuated loss of contractile and pump function.[9] Alongside this, an inflammatory reaction will also occur by motivating the migration of macrophages to the myocardium,[10] mainly through macrophage 1 and 2. Macrophage activity will be rich in several growth factors and cytokines.[10,11]

Methods

In this narrative review, an analytical framework was adopted to synthesize and evaluate the findings from the literature, aiming to depict the chain of logic, as evidence must support possible future clinical outcomes. To refine the investigation, a comprehensive search strategy was employed to identify relevant literature sources, utilizing specific Medical Subject Headings (MeSH) terms provided by the National Library of Medicine (NLM). These terms included Myocardial Ischemia, Coronary Artery Disease, FSTL-1, Follistatin-Related Proteins, and Follistatin-Related Protein 1. The primary databases utilized for the literature search included PubMed, Scopus, and Web of Science, with a focus on articles published between January 2000 and May 2022 to capture the most recent advancements in the field.

The inclusion criteria for this narrative review were rigorously defined to ensure a comprehensive and relevant synthesis of existing literature on FSTL-1 in cardiac regeneration. Eligible studies included peer-reviewed observational and interventional studies, reviews, meta-analyses, and both molecular and animal model studies, all published in English between January 2000 and May 2022. The focus on studies published within this timeframe was chosen to capture the most relevant and contemporary research, reflecting the significant advancements in the understanding of FSTL-1 over the past two decades. This period was selected because it encompasses the critical years during which FSTL-1 emerged as a potential therapeutic target, as well as the development of advanced molecular techniques and animal models that have provided deeper insights into its biological functions. By concentrating on this timeframe, the review aims to highlight the progression of scientific knowledge and the most current perspectives on FSTL-1's role in cardiac regeneration, ensuring that the findings are both up-to-date and aligned with the latest research trends.

Selection was based on the studies' contributions to elucidating FSTL-1's mechanisms within human physiology, with particular emphasis on research that provided clear and significant insights into its role in cardiovascular regeneration. To ensure that the included studies were of high relevance and scientific rigor, only those that adhered to established principles of biomedical research were considered. This included studies employing robust methodologies, validated models, and those that used precise and accepted scientific terminology, ensuring the findings could be interpreted accurately by medical students and professionals alike.

Additionally, studies were omitted if their methodologies were found to be flawed or if their findings did not align with the broader body of evidence on FSTL-1. Methodological flaws that led to exclusion included issues such as small sample sizes, inadequate controls, lack of reproducibility, and insufficient statistical power, all of which could compromise the validity and reliability of the findings. Studies with discrepancies or inconsistencies when compared to the established scientific consensus on FSTL-1 were also excluded. This approach was taken to ensure that the review presents a cohesive and scientifically sound narrative, grounded in evidence that is both credible and widely accepted by the research community. By filtering out studies with methodological weaknesses or conflicting results, the review aims to provide a clear and accurate synthesis of the current state of knowledge on FSTL-1, thereby offering reliable insights into its potential therapeutic applications.

The synthesis of findings followed a structured narrative approach, enabling a qualitative analysis that integrated diverse types of evidence to construct a cohesive overview of FSTL-1's role in cardiovascular regeneration. The narrative was developed chronologically, reflecting the evolution of scientific knowledge from fundamental concepts to advanced animal models and potential clinical applications, thereby providing a clear and logical progression of the field's development.

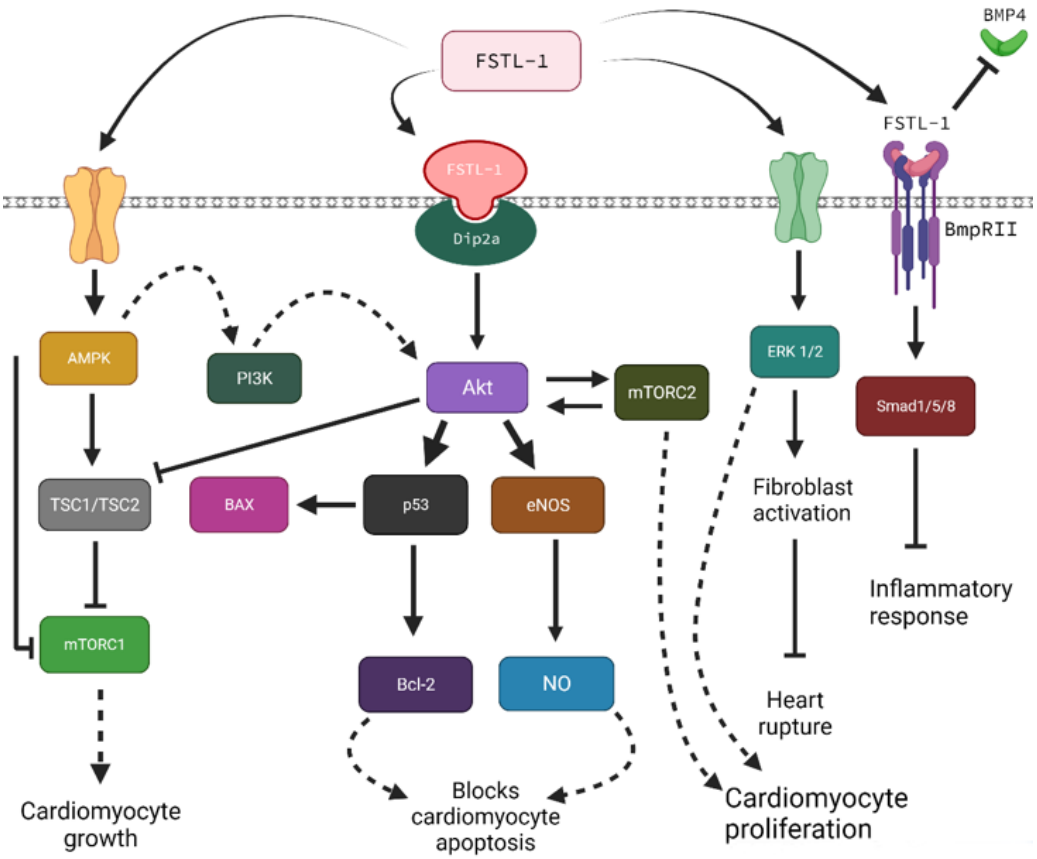
Results

FSTL-1 in the Heart

The most prominent regulation mechanism by FSTL-1 is the serine/threonine protein kinase (AKT), also known as phosphatidylinositol 3-kinase (PI3K). AKT has been identified as a key piece in myocardial growth induced by stress (Fig.1).[12,13] Investigation of AMP-activated protein kinase (AMPK) has also been conducted and discovered to safeguard cardiomyocytes from apoptosis during a MI.[14,15] This is due to the capacity of FSTL-1 to stimulate the phosphorylation of AMPK Thr172.[14] Research has proven that FSTL-1 overexpression would lead to an upregulation of both an AKT and ERK signalling in cardiac myocytes, resulting in better survival rates under hypoxic conditions and induced apoptosis.[16] This correlates with previous research, as AKT and ERK are positively correlated with cellular survival.[17,18,19] Other pro-survival factors include Pim-1, hypoxia-inducible factor-1α, and heme-oxygenase-1, which are also involved in the AKT signalling mechanism, although their relationship and function are still not understood in their entirety.[20,21] Meanwhile, ERK signalling seems to occur mainly in cardiac fibroblasts, with its central purpose being the proliferation and migration of the same cells. It is hypothesized that the controlled fibrotic reaction offered by FSTL-1 derives from an early activation and migration of cardiac fibroblasts, which in turn will lead to a greater myofibroblast build-up in the infarcted area.[22] This is believed to allow for an improved synthesis and maturing of extracellular matrix in the affected zone.[14] This reasoning is well-based, as FSTL-1 largely resembles the SPARC family, which is an initial controller of extracellular matrix maturation after MI.[23] Although alternative pathways to that proposed by Murayama et al. might also exist in relation to the activation of FSTL-1. As it has been demonstrated that fibroblasts are responsible for activating the Smad2/3 signalling route via TGF-β1 which will cause a fibrotic response.[22]

Bone morphogenic protein-4 (BMP4) has also been shown to boost the apoptosis of cardiomyocytes.[23] BMP4 is one of the commonly released proteins during an inflammatory response to MI[24,25] and is related to an enhanced phosphorylation of the previously mentioned Smad1/5/8 signalling, as shown in ***Figure 1***. Reports have been conducted where they showed that FSTL-1 would bind to BPM4[26], which would inhibit further activity.[14,27]

Figure 1. Visual Representation of the Discussed FSTL-1 Stimulated Pathways.



Legend: AMPK, AMP-Activated Protein Kinase; PI3K, Phosphoinositide 3-Kinase; TSC1/2, Tuberous Sclerosis Complex 1/2; mTORC1/C2, Mammalian Target of Rapamycin Complex1/2; DIP2A, Disco-Interacting Protein 2 Homolog A; Akt, Protein Kinase B; BAX, Bcl-2 Associated X-protein; eNOS, Endothelial Nitric Oxide Synthase; NO, Nitric Oxide; ERK, Extracellular Signal-Regulated Kinase; BMP-4, Bone Morphogenetic Protein-4.

Inflammatory Response

Macrophages are the main source of proinflammatory cytokines during MI.[28,29] Cytokines such as IFNγ and IL-1β will increase the secretion of FSTL-1. Other cytokines are responsible for increased levels of tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6). BMP4 is largely known for its increase in the expression of TNF-α and IL-6 after MI, resulting in an exaggerated and prejudicial inflammation of cardiac tissue. Due to the inhibition of BMP4 by FSTL-1 (Fig.1), inflammatory processes are considerably decreased, thus proving that FSTL-1 is a strong anti-inflammatory in post-MI.[14] AMPK signalling, dependent on FSTL-1, has also been linked to an inhibition of macrophage migration (Fig.1).[15] FSTL-1 also decreased lipopolysaccharide-stimulated expression of proinflammatory genes via activation of AMPK.[14]

Real-World Response

In a forerunner investigation by Wei et al., FSTL-1 was introduced to the epicardium through a nanofibrillar collagen patch.[34] It proved some different short-term effects, including reduced fibrosis and increased vascularisation beneath and surrounding the epicardial patch. Measurements showed an increase in the number and size of blood vessels. It is believed one of the processes behind revascularisation depends on a nitric-oxide process, which is most likely regulated by a paracrine mechanism.[30] Cardioprotection also occurred, as embryonic stem cell-derived cardiomyocytes did not undergo apoptosis provoked by the hypoxic environment, which is in correlation with previous studies.[16,30]

Wei et al. also proved that it could have mid-term effects, as after a 4-week period, the area beneath the patch showed striated myocytes, and in the border zones of the patch, cardiomyocytes had also undergone cell division, which proved that FSTL-1 had successfully induced cell cycle entry and cytokine release.[33] However, Chen et al. also showed that FSTL-1 can be used to incentivise the proliferation of mature adult ventricular cardiomyocytes, as it did not induce synthesisation of DNA or division as well as hypertrophy, showing some limitations in this aspect.[34] Thus, clear knowledge gaps still remain, as currently it is still unknown if these cells originate *de novo* or from pre-existing cardiomyocytes. Studies have been conducted in this regard, as fate mapping indicated that resident cardiomyocytes were the main source of regeneration in the myocardium. However, during the investigation, a small percentage of cardiomyocytes didn't undergo labelling, suggesting an alternative source of cardiomyocytes.[35] Current evidence points that this unknown source is most likely made up of ckit+ cells, as it was found that they can also contribute to the proliferation and regeneration of cardiomyocytes after MI.[36]

Probably the most pertinent issue that came from Wei et al. was the difference between FSTL-1 expression in the myocardium *vs.* the epicardium. The overexpression of myocardial FSTL-1 varied in its role in comparison to the overexpression of FSTL-1 in the epicardium. The initial idea behind this discrepancy was that there were differences in the migration rates of the cells due to differing glycosylation processes. FSTL-1 produced from different cellular sources are most likely exposed to differences in the post-translational glycosylation, which will inevitably result in varying isoforms.[37] FSTL-1 derived from the myocardium demonstrated cardioprotective functions but not cardio regenerative.[38] While FSTL-1 derived from the epicardium demonstrated a cardio regenerative capacity.[38] Other studies showed that non-glycosylated FSTL-1 increases the proliferation of cardiomyocytes, while glycosylated FSTL-1 protects cardiomyocytes from peroxidase-induced apoptosis.[38] However, other factors might also be influencing the activation processes and subsequent role of FSTL-1. Maruyama et al. in a more recent investigation, explored this topic as they evaluated the effect of glycosylation of FSTL-1 in relation to cardiac fibroblast activation.[39] For this, they used insect, mammalian, and bacteria cells. Although the glycosylation mechanisms varied substantially between the three, there were no statistically significant differences in the capacity of each FSTL-1 protein to promote activation of cardiac fibroblasts and their role.[39]

Other areas of interest revolve around the relationship of FSTL-1 with other peptides, such as thymosin β4, due to their similarities, such as the production of epicardial-derived cells and a strong driving force of angiogenesis and mobilization.[38] Thymosin β4 has already been reported as a strong pro-vasculogenic factor.[40] Following MI, thymosin β4 has been shown to induce epicardial-derived cells to form vascular precursors and prompt angiogenesis in the human heart.[41] Further investigation has established a relationship between thymosin β4 and the capacity of Wt1+ cells to undertake cardiomyogenesis.[40,42]

Alongside this, FSTL-1 has been proven to inhibit the entrance into the apoptotic mode of cardiomyocytes. Akt/GSK-3β signalling was verified in hypoxic-FSTL-1 cells, being currently held as the main mechanism behind anti-apoptosis in hypoxic conditions. More technical analyses have also shown that the heart upregulated FSTL-1 expression under mechanical stresses such as pressure.[34] Due to these cardioprotective roles, cardiac tissue, under the presence of FSTL-1, can be able to positively regulate the cardiac microenvironment and induce the importation or production of pro-regenerative substances.[34] This regulation post-MI is managed by elements such as retinoic acid, hypoxia-inducing factor-1α, fibroblast growth factors, transforming growth factor-beta (TGFβ), insulin-like growth factor, and BMP, among many others.[43]

Musculoskeletal Secretion

FSTL-1 produced outside the heart is also essential in post-MI scenarios, as skeletal muscle is the main producer of circulating FSTL-1 and has been linked to transgenic AKT-1 overexpression.[44] Circulating FSTL-1 will resemble a myokine by maintaining its previously reported cardioprotective role through an endocrine method.[45] Increased myocardium angiogenesis and an overall increase in the heart's performance were reported due to an augmented TGFβ-Smad2/3 signalling (Fig.1).[45,46] Reduced levels of FSTL-1 in the blood have also been shown to be correlated to more prominent inflammatory reactions in arterial injury.[46] FSTL-1 will also inhibit the proliferation and migration of smooth muscle cells in damaged blood vessels, which will lower the effect of neointimal hyperplasia after vascular injury.[45] This will result in the control of smooth muscle cells through the stimulation of AMPK mechanisms through an increase in phosphorylation.[45] Exercise is essential as it increases FSTL-1 expression in skeletal muscle, especially through intermittent aerobic exercise.[46] This is further emphasised as circulating FSTL-1 would increase its expression in the heart's myocardium heart, which is a strong indicator of regulation through positive feedback.[45] FSTL-1 has also been tested in conjunction with mesenchymal stem cells due to the inherent characteristics FSTL-1 possess.[30] This was an attempt at addressing some of the issues currently associated with cardiac stem cell therapy, mainly low survival percentage and difficulty in retention and engraftment of donor cells in ischemic tissue.[7] A study by Shen et al. showed promise in this hypothesis, as FSTL-1 successfully enhanced the resistance of mesenchymal stem cells to hypoxia, a reduction in fibrosis, inflammatory cell infiltration and an increase in neovascularisation.[30] The production of extracellular matrix was also considerably modulated, as tested by western blot analysis, which showed that mesenchymal stem cells injected in conjunction with FSTL-1 decreased the transcription rates of collagen type I and fibronectin in peri-infarcted zones. Other pro-fibrogenesis cytokines, such as connective tissue growth factor, decreased in ischaemic myocardium.[30]

Discussion

In evaluating the limitations of the studies encompassed within this review, several critical considerations emerge that significantly influence the interpretation of findings and the broader understanding of FSTL-1's role in cardiac regeneration. A primary concern is the diverse methodologies and experimental models employed across these studies. Animal models, such as rodents and larger mammals, have been invaluable in elucidating the molecular mechanisms underpinning cardiac regeneration. However, the translational relevance of these findings to human physiology remains a complex challenge. Differences in cardiac anatomy, physiology, and regenerative capacity between species necessitate cautious extrapolation of preclinical data. Many investigations have provided valuable insights into the molecular pathways involving FSTL-1 in cardiac regeneration, a predominant focus on mechanistic aspects without sufficient consideration of direct clinical relevance or translational implications limits the practical utility of these findings. Additionally, the heterogeneity in experimental protocols—ranging from dosing regimens and delivery methods to the timing of interventions—introduces variability that complicates the interpretation and comparison of results across studies. This emphasis on fundamental research, though crucial for understanding underlying biological mechanisms, can often fail to address the practical challenges of translating FSTL-1-based interventions into clinically effective therapies. The absence of comprehensive preclinical studies that integrate mechanistic insights with translational endpoints—such as functional recovery and long-term safety assessments—represents a significant gap in the literature.

Furthermore, publication bias poses a significant challenge in the existing literature. Studies reporting positive outcomes or novel findings are more likely to be published, potentially leading to an overrepresentation of favorable results. Conversely, studies with neutral or negative findings may face greater difficulties in publication, resulting in an underrepresentation of valuable data. This bias can skew the overall perception of FSTL-1's therapeutic potential, either fostering unwarranted enthusiasm or undue skepticism.

In addition to the aforementioned points, the integration of FSTL-1 into complementary therapeutic approaches, such as mesenchymal stem cell therapy, holds promise for optimizing cardiac regeneration strategies. Leveraging the epicardium as a targeted cell therapy site represents a compelling avenue for enhancing the efficacy of regenerative interventions. However, to fully capitalize on this potential synergy, a comprehensive understanding of the intricate molecular networks governing cardiac regeneration is essential. These networks, characterized by intricate interplay and feedback loops, involve not only FSTL-1 but also other cardio-protective and regenerative proteins expressed in the myocardium. Despite significant progress in elucidating the mechanisms regulated by FSTL-1, gaps persist, particularly regarding the upstream activators of FSTL-1 expression. Resolving these knowledge gaps is critical for developing precise therapeutic interventions. Furthermore, while recent studies have shed light on FSTL-1's role in modulating immune responses post-MI, further research in this direction is warranted to unravel its full therapeutic potential.

Moreover, fostering interdisciplinary collaborations and aligning research efforts with emerging trends in cardiovascular science is paramount. Recent advancements in stem cell therapy, including investigations into c-kit+ cells and Wt1+ cells, present opportunities to address existing challenges, such as poor engraftment of donor cells in hypoxic environments. Exploring the secretion of FSTL-1 in skeletal muscle and its implications for cardiac rehabilitation post-MI or post-op represent another intriguing avenue for future exploration. By capitalizing on synergies between diverse therapeutic modalities and integrating novel insights from related fields, we can unlock new dimensions

in cardiac regeneration and pave the way for transformative advancements in cardiovascular medicine.

However, despite the overall agreement on FSTL-1's beneficial effects in cardiac regeneration, there are notable discrepancies and contradictions in some areas of the literature. For instance, while some studies demonstrate a clear cardioprotective role for FSTL-1[33], others suggest no significant impact on cardiac function when acting alone.[44] Additionally, discrepancies exist regarding the mechanisms underlying FSTL-1 mediated cardiomyocyte proliferation, with some studies implying activation of specific signaling pathways, such as AKT and ERK, while others propose alternative mechanisms.

Furthermore, contradictory findings are observed regarding the optimal timing and dosage of FSTL-1 administration for maximal therapeutic efficacy. Some studies suggest that early administration of FSTL-1 post-injury is more effective in promoting cardiac regeneration[33], while others advocate for delayed intervention to allow for resolution of inflammation and scar formation before initiating regenerative processes.[5] Similarly, discrepancies exist regarding the source of FSTL-1 secretion and its precise cellular targets within the myocardium, highlighting the need for further investigation to elucidate these aspects.

Despite these advances in understanding FSTL-1, it is important to note that, as of now, there are no clinical trials involving FSTL-1 in cardiac regeneration. However, the future setup of such trials could involve carefully designed, phased approaches to assess safety, dosage, timing, and efficacy. Initial trials might focus on determining the optimal delivery method of FSTL-1, such as direct injection into the myocardium or incorporation into biomaterials used in cardiac patches. These trials could also investigate the timing of administration relative to myocardial infarction or surgical intervention, as well as the integration of FSTL-1 with other therapies, such as stem cell treatments or pharmacological agents. Subsequent trials would likely expand to larger populations and longer follow-up periods to fully assess long-term outcomes and potential benefits in preventing heart failure or improving functional recovery post-MI. As research progresses and a deeper understanding of FSTL-1's role in cardiac regeneration emerges, clinical trials will play a pivotal role in translating these findings into viable therapeutic strategies.

Conclusion

The key findings from our review underscore the significant role of FSTL-1 as a stable and effective cardio-protective and regenerative factor in cardiovascular research. FSTL-1's multifaceted mechanisms demonstrate considerable potential in addressing critical clinical challenges in MI treatment, such as the clearance of necrotic tissue, restoration of lost cardiomyocytes, regeneration of electrical conductivity, and resolution of inflammation and fibrotic tissue accumulation. Notably, our review highlights the importance of optimizing FSTL-1 delivery methods—whether through intravenous administration or via a nanofibrillar collagen patch—both of which hold promise for enhancing the efficacy of therapeutic interventions and improving the quality of engrafted cells.

In the broader context of cardiovascular therapy, FSTL-1 emerges as a highly promising therapeutic target with the potential to revolutionize clinical approaches to MI and other cardiac conditions. The elucidation of FSTL-1's molecular mechanisms provides a foundation for its integration into innovative treatment strategies, potentially transforming current practices in cardiac care. Clinically, FSTL-1 offers avenues for developing targeted therapies that could mitigate heart damage, promote tissue regeneration, and improve long-term outcomes for patients. The versatility of FSTL-1 in addressing multiple facets of cardiac injury suggests that it could be pivotal in creating personalized and precision-based treatments, particularly in high-risk patient populations.

As research continues to delve into the complexities of FSTL-1's actions and refine its delivery systems, the potential for FSTL-1 to serve as a cornerstone in cardiovascular medicine becomes increasingly evident. With further development, FSTL-1 could lead to groundbreaking therapies that significantly enhance patient recovery and survival rates, marking a substantial advancement in the clinical management of MI and related cardiac disorders.

Summary – Accelerating Translation

Follistatin-like 1 and its application in Ischaemic Heart Disease

FSTL-1 is a protein that has gained significant attention in the field of cardiac rejuvenation due to its crucial role in promoting cardiac tissue repair and regeneration. This study has as its main aim to identify, understand and summarise the molecular and immune-physiological mechanisms underpinning this molecule and how it they might apply to cardiac regeneration. Through this narrative review, the aim was to synthesise information from various sources on this topic in a descriptive and/or qualitative manner, with a more flexible and holistic overview of the existing literature.

FSTL-1 has been identified as a key player in this subject because of its ability to stimulate the growth and repair of heart muscle tissue. This is of great importance because the heart has limited regenerative capacity, and injuries or diseases can lead to irreversible damage. FSTL-1 has also been found to activate cardiac stem cells and promote their differentiation into functional cardiac muscle cells (cardiomyocytes). This process is vital for replenishing damaged or dead cells in the heart after injury, such as a heart attack. FSTL-1 exhibits anti-inflammatory properties by modulating the immune response. Inflammation is a major contributor to heart damage following cardiac events. By reducing inflammation, FSTL-1 helps create a more favorable environment for cardiac repair. Another critical aspect of cardiac regeneration is the formation of new blood vessels (angiogenesis) to supply oxygen and nutrients to regenerating tissue. FSTL-1 has been shown to promote angiogenesis in the heart, facilitating the healing process. FSTL-1 may also help reduce fibrosis, the excessive formation of scar tissue in the heart, which can impair cardiac function. By limiting fibrosis, FSTL-1 aids in preserving and restoring the heart's contractile function.

Understanding the importance of FSTL-1 in cardiac regeneration holds significant promise for the development of novel therapeutic approaches for heart disease treatment. Researchers are exploring ways to harness the regenerative potential of FSTL-1, such as through gene therapy or the development of pharmaceutical agents that mimic its effects.

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Acknowledgments

My thanks to Dr. Mário Santos, as my mentor and experienced cardiologist, he had the chance to do a review of the overall manuscript.

Conflict of Interest Statement & Funding

The Authors have no funding, financial relationships or conflicts of interest to disclose.

Author Contributions

Conceptualization: JRG. Investigation: JRG. Writing - Review Editing: JRG.

Cite as

Gomes J. A Narrative Review on the FSTL-1 Protein and its Current Known Impact on Cardiovascular Ischaemic Disease. Int J Med Stud. 2024 Oct-Dec;12(4):457-464.

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ISSN 2076-6327

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