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The Potential of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), Gene Editing Technology, in the Treatment of Coronary Artery Disease: A Systematic Literature Review

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A B S T R A C T

The treatment of CAD depends on the severity of the disease and the individual's risk factors. There are a number of medications that can help to slow the progression of CAD and reduce the risk of complications. The treatments for CAD can have side effects, which can make it difficult for people to adhere to their treatment plan. The treatments for CAD can be expensive, which can make it difficult for people to afford them. This is especially true for people who do not have insurance. This study aimed to conduct a systematic review to explore the potential of CRISPR in CAD management. The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the potential of CRISPR in the treatment of coronary artery disease. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations. CRISPR has great potential as a future therapeutic modality for coronary artery disease, where this technology is able to control various CAD risk factors and can trigger the formation of new blood vessels to overcome coronary artery blockade. However, this very potential technology still requires ethical concern studies in order to be able to maintain human sustainability.

1. Introduction

Coronary artery disease (CAD) is a condition in which the arteries that supply blood to the heart become narrowed or blocked. This can lead to chest pain, heart attack, and other serious complications. The narrowing or blockage of the arteries is caused by a buildup of plaque, which is a combination of cholesterol, fat, calcium, and other substances. As plaque builds up, it can reduce the amount of blood that flows through the arteries. This can lead to chest pain (angina) when the heart muscle doesn't get enough oxygen. If a plaque ruptures, it can form a blood clot that blocks the artery completely. This can lead to a heart attack. CAD is a major risk factor for heart attack, stroke, and other cardiovascular diseases.[1-3]

The treatment of CAD depends on the severity of the disease and the individual's risk factors. There are a number of medications that can help to slow the progression of CAD and reduce the risk of complications. These medications include cholesterol-lowering drugs, blood pressure medications, and aspirin. Making lifestyle changes can also help to improve the symptoms of CAD and reduce the risk of complications. These changes include eating a healthy diet, exercising regularly, maintaining a healthy weight, and quitting smoking. In some cases, procedures may be necessary to open blocked arteries

or bypass blocked arteries. These procedures include angioplasty, coronary artery bypass grafting (CABG), and transcatheter aortic valve replacement (TAVR). The treatments for CAD can have side effects, which can make it difficult for people to adhere to their treatment plan. For example, statins can cause muscle pain, and beta-blockers can cause fatigue. The treatments for CAD can be expensive, which can make it difficult for people to afford them. This is especially true for people who do not have insurance.[4,5]

CRISPR, which stands for Clustered Regularly Interspaced Short Palindromic Repeats, is a gene editing technology that allows scientists to make precise changes to DNA. CRISPR was adapted for use in the laboratory from naturally occurring genome editing systems found in bacteria. CRISPR works by using a guide RNA to target a specific sequence of DNA. The guide RNA is a short piece of RNA that is complementary to the target DNA sequence. When the guide RNA binds to the target DNA sequence, it recruits a protein called Cas9, which cuts the DNA at that location. The CRISPR-Cas9 system can be used to make a variety of changes to DNA, including Cleaving DNA: This is the most basic function of CRISPR-Cas9. It can be used to remove a specific sequence of DNA or to create a break in the DNA that other proteins can repair. Inserting DNA: CRISPR-Cas9 can be used to insert a new sequence of DNA into a specific location in the genome. This can be used to repair a mutation or to introduce a new gene into the genome. Modifying DNA: CRISPR-Cas9 can be used to modify the sequence of DNA at a specific location. This can be used to change a single base pair or to insert or delete larger sections of DNA.[6,7]

CRISPR has the potential to revolutionize the treatment of coronary artery disease (CAD). CRISPR could be used to treat CAD in a number of ways. Correct mutations in genes that are known to be involved in CAD. For example, CRISPR could be used to correct mutations in the LDLR gene, which is responsible for producing LDL receptors. LDL receptors help remove cholesterol from the blood, so mutations in the LDLR gene can lead to high cholesterol levels, which are a major risk factor for CAD. Inactivate genes that promote the growth of plaque in the arteries. For example, CRISPR could be used to inactivate the MCP-1 gene, which is responsible for producing a protein that promotes the growth of plaque in the arteries. Inactivating the MCP-1 gene could help to prevent the formation of plaque and reduce the risk of CAD. Promote the growth of new blood vessels to bypass blocked arteries. This could be used to bypass blocked arteries and improve blood flow to the heart.[7,8] This study aimed to conduct a systematic review to explore the potential of CRISPR in CAD management.

2. Methods

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the potential of CRISPR in the treatment of coronary artery disease. The search was performed using the terms: (1) "CRISPR" OR "Gene Editing Technology," OR "Gene Technology" OR "CAD" AND (2) "CRISPR" OR "Coronary Disease." The literature is limited to observational studies and published in English. The literature selection criteria are articles published in the form of original articles, an experimental study about the potential of CRISPR in the treatment of coronary artery disease, studies were conducted in a timeframe from 2013-2023, and the main outcome was the potential of CRISPR in treatment of coronary artery disease. Meanwhile, the exclusion criteria were the studies that were not related to the potential of CRISPR in the treatment of coronary artery disease, the absence of a control group, and the duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

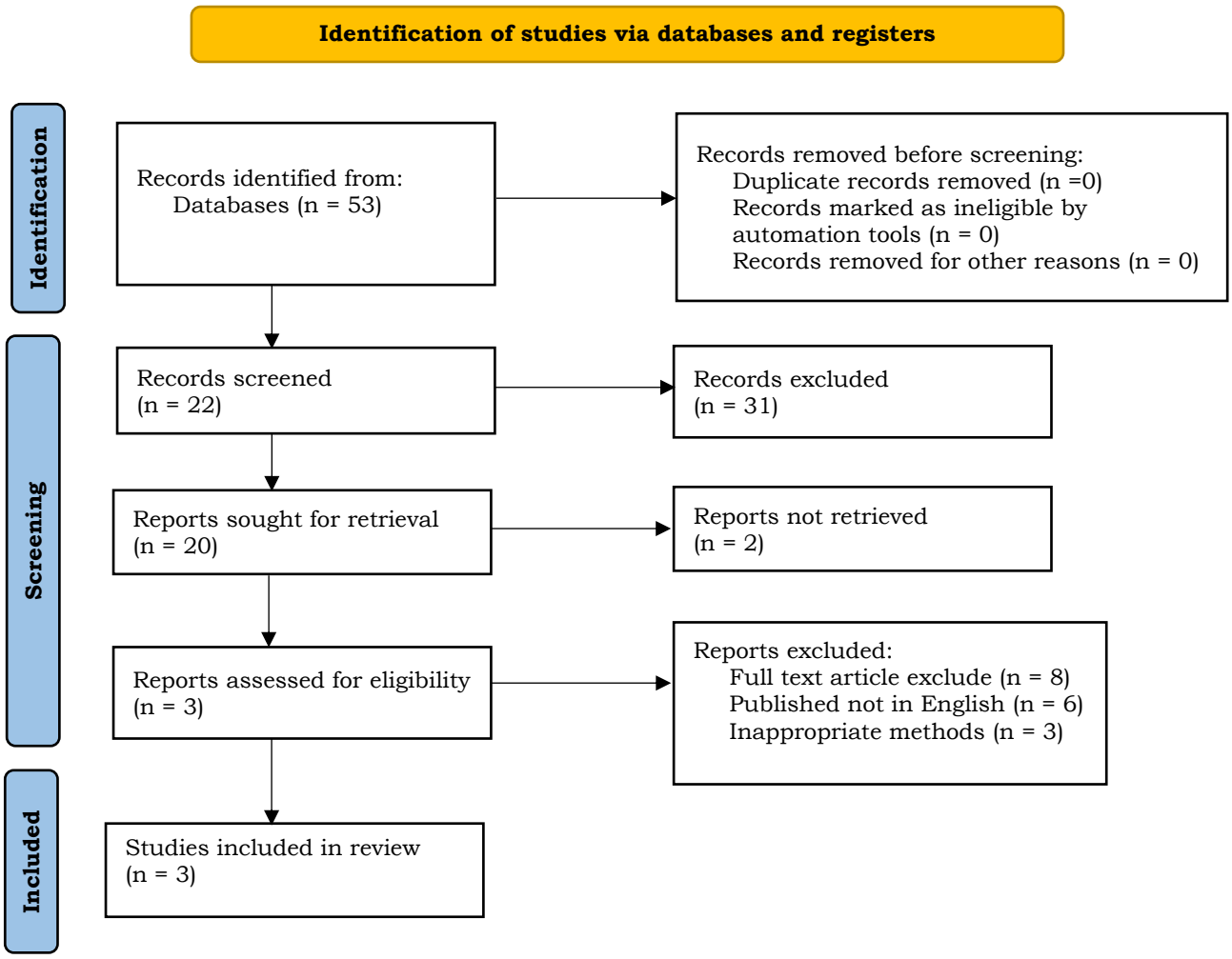

Figure 1. Research PRISMA diagram.

3. Results and Discussion

CRISPR, gene editing technology

CRISPR gene editing technology is a revolutionary new way to change the DNA of living organisms. It is based on a natural defense system that bacteria use to protect themselves from viruses. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. These are short sequences of DNA that are found in bacteria and archaea. They are interspersed with short sequences of non-coding DNA. The system consists of two parts: a guide RNA and the Cas9 protein. The guide RNA is a short piece of RNA that is complementary to the target DNA sequence. It is designed to find and bind to a specific sequence of DNA in the cell. Once the guide RNA has found the target sequence, it binds to it and recruits the Cas9 protein. The Cas9 protein is an enzyme that cuts DNA. It is activated by the guide RNA and cuts the DNA at the target site. This cut in the DNA can then be repaired in a number of ways. One way is to leave the cut as it is simple. This will prevent the gene from being expressed. Another way is to repair the cut by inserting a new piece of DNA. This can be used to add, remove, or change genes.[9]

The CRISPR-Cas9 system works by first finding a specific sequence of DNA in the cell. This is done using a guide RNA, which is a short piece of RNA that is complementary to the target DNA sequence. Once the guide RNA has found the target sequence, it binds to it and recruits the Cas9 protein. The Cas9 protein then cuts the DNA at the target site.[10] This cut in the DNA can then be repaired in a number of ways. One way is to leave the cut as it is simple. This will prevent the gene from being expressed. Another way is to repair the cut by inserting a new piece of DNA. This can be used to add, remove, or change genes. The way the

DNA is repaired after being cut by Cas9 determines the outcome of the CRISPR gene editing process. There are two main ways that DNA can be repaired after being cut by Cas9: Non-homologous end joining (NHEJ): This is the most common way that DNA is repaired after being cut by Cas9. In NHEJ, the cell simply joins the two ends of the DNA back together without any additional DNA. This can lead to small insertions or deletions in the DNA, which can change the expression of the gene. Homology-directed repair (HDR): HDR is a more precise way to repair DNA after being cut by Cas9. In HDR, the cell uses a piece of donor DNA that is homologous to the target DNA to repair the cut. This can be used to add, remove, or change genes.[11]

The choice of which repair pathway to use depends on a number of factors, including the location of the cut in the DNA and the availability of a donor DNA template. NHEJ is a faster and more efficient way to repair DNA than HDR. However, NHEJ is more likely to lead to errors, such as small insertions or deletions in the DNA. HDR is a slower and less efficient way to repair DNA than NHEJ. However, HDR is more precise and less likely to lead to errors. The choice of which repair pathway to use depends on the specific application of CRISPR gene editing. For example, if the goal is to silence a gene simply, then NHEJ may be a good choice. However, if the goal is to change the sequence of a gene precisely, then HDR may be a better choice.[12]

Correct mutations in genes that are known to be involved in CAD

CRISPR gene editing could be used to correct mutations in genes that are known to be involved in CAD. For example, CRISPR could be used to correct mutations in the LDLR gene, which is responsible for producing LDL receptors. LDL receptors help remove cholesterol from the blood, so mutations in the LDLR gene can lead to high cholesterol levels, which are a major risk factor for CAD. In addition to the LDLR gene, there are a number of other genes that are known to be involved in CAD. These include the APOB gene, which is responsible for producing apolipoprotein B; the PCSK9 gene, which is involved in the metabolism of LDL cholesterol; and the SORT1 gene, which is involved in the transport of LDL cholesterol out of cells.[13]

The APOB gene is responsible for producing apolipoprotein B, which is a protein that is found in LDL cholesterol particles. LDL cholesterol is a type of cholesterol that is known to build up in the arteries and cause CAD. Mutations in the APOB gene can lead to high levels of LDL cholesterol, which increases the risk of CAD. The PCSK9 gene is involved in the metabolism of LDL cholesterol. PCSK9 is a protein that binds to LDL receptors and helps to remove LDL cholesterol from the blood. Mutations in the PCSK9 gene can lead to low levels of LDL receptors, which increases the risk of CAD. The SORT1 gene is involved in the transport of LDL cholesterol out of cells. SORT1 is a protein that helps to transport LDL cholesterol out of cells and into the bloodstream. Mutations in the SORT1 gene can lead to high levels of LDL cholesterol in the cells, which increases the risk of CAD. The LDLR gene is responsible for producing LDL receptors. LDL receptors are proteins that are found on the surface of cells. They bind to LDL cholesterol particles and help to remove them from the blood. Mutations in the LDLR gene can lead to low levels of LDL receptors, which increases the risk of CAD. The ABCA1 gene is involved in the transport of cholesterol out of cells. ABCA1 is a protein that helps to transport cholesterol out of cells and into the bloodstream. Mutations in the ABCA1 gene can lead to high levels of cholesterol in the cells, which increases the risk of CAD. The HMGCR gene is involved in the production of cholesterol. HMGCR is an enzyme that is involved in the synthesis of cholesterol. Mutations in the HMGCR gene can lead to high levels of cholesterol in the blood, which increases the risk of CAD.[14,15]

CRISPR gene editing could be used to correct mutations in any of these genes

CRISPR gene editing could be used to correct mutations in any of these genes. This could help to prevent or treat CAD in people who are at risk for the

disease. Inactivate genes that promote the growth of plaque in the arteries. For example, CRISPR could be used to inactivate the MCP-1 gene, which is responsible for producing a protein that promotes the growth of plaque in the arteries. Inactivating the MCP-1 gene could help to prevent the formation of plaque and reduce the risk of CAD.[16]

MCP-1 is a gene that codes for a protein called monocyte chemoattractant protein-1. This protein is involved in the recruitment of immune cells to sites of inflammation. In the context of CAD, MCP-1 can promote the growth of plaque in the arteries by attracting immune cells to the site of inflammation. CRISPR gene editing could be used to inactivate the MCP-1 gene. This would prevent the production of monocyte chemoattractant protein-1, which would, in turn, reduce the recruitment of immune cells to the site of inflammation. This could help to prevent the growth of plaque and reduce the risk of CAD.[17]

Promote the growth of new blood vessels to bypass blocked arteries.

CRISPR gene editing could be used to promote the growth of new blood vessels to bypass blocked arteries. This could be used to bypass blocked arteries and improve blood flow to the heart. One way that CRISPR gene editing could be used to promote the growth of new blood vessels is by targeting the gene for vascular endothelial growth factor (VEGF). VEGF is a protein that is involved in the growth of new blood vessels. CRISPR gene editing could be used to increase the expression of VEGF, which would, in turn, promote the growth of new blood vessels.[18]

Another way that CRISPR gene editing could be used to promote the growth of new blood vessels is by targeting the gene for angiopoietin-1. Angiopoietin-1 is a protein that is involved in the stabilization of new blood vessels. CRISPR gene editing could be used to increase the expression of angiopoietin-1, which would, in turn, help to stabilize new blood vessels and prevent them from regressing.[19]

Ethical concerns of CRISPR

CRISPR gene editing is a powerful new technology that has the potential to revolutionize medicine. However, it also raises a number of ethical concerns. One of the main ethical concerns about CRISPR gene editing is the potential for unintended side effects. CRISPR gene editing is a very precise technology, but it is not perfect. There is always the possibility that CRISPR gene editing could accidentally alter the wrong gene or cause other unintended changes to the genome. Another ethical concern about CRISPR gene editing is the potential for discrimination. If CRISPR gene editing is used to create designer babies, there is a risk that people with certain genetic traits will be discriminated against. For example, people with genetic traits that are associated with diseases or disabilities may be less likely to be hired or insured.[20]

There is also the ethical concern of who should have access to CRISPR gene editing. CRISPR gene editing is a very expensive technology, and it is not clear who will be able to afford it. This could lead to a situation where only the wealthy have access to CRISPR gene editing, which could widen the gap between the rich and the poor. Finally, there is the ethical concern of whether it is right to alter the human genome. Some people believe that it is wrong to tamper with the natural order of things and that CRISPR gene editing could lead to unforeseen consequences.

These are just some of the ethical concerns that need to be considered before CRISPR gene editing can be used in humans. It is important to have a public discussion about these issues so that we can make informed decisions about the future of CRISPR gene editing.

4. Conclusion

CRISPR has great potential as a future therapeutic modality for coronary artery disease, where this technology is able to control various CAD risk factors and can trigger the formation of new blood vessels to overcome coronary artery blockade. However, this very potential technology still requires ethical concern

studies in order to be able to maintain human sustainability.

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