CRISPR-Cas9 as Treatment for HIV

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INTRODUCTION

HIV is a chronic/life-long infection that is transmitted through bodily fluids and is specifically associated with sexual activity. Although the prevalence of HIV is high, there is currently no curative treatment.[1] Current therapies are directed at suppressing the viral load in infected individuals, reducing transmission risk and progression to AIDs. Unfortunately, this is not equivalent to eradication, and patients must remain on these medications for life. These medications require strict adherence for efficacy and have an estimated lifetime cost of ~ $379,668 ($23,000 per year).[2] Overall, it has been demonstrated that those with HIV continue to have substantially lower health-related quality of life than the general population due to a multitude of reasons for which CRISPR-Cas9 may serve as a potential solution.[3]

The CRISPR-CAS9 system was originally discovered in the prokaryotic immune response. It is comparable to the human immune response in that it creates memory to foreign genetic material, but in the form of spacers rather than antibodies. When the prokaryote recognizes reinvasion by the same species, a select CRISPR RNA (crRNA) is processed and used to locate and bind the invader. Once bound, the Cas9 enzyme cuts and deactivates it.[4] Researchers have been able to reproduce this system in the lab. Once the foreign or mutated DNA is cut, researchers use the cell's own DNA repair machinery to add/delete pieces of genetic material, or to make changes to the DNA by replacing an existing segment with a customized DNA sequence.[5] Therefore, researchers are looking into the ways in which this system can be used to completely eradicate the HIV genome from infected individuals, thereby improving their quality of life and subsequently reducing the incidence of HIV in the US.

OBJECTIVE

The objective of this literature review is to determine if the CRISPR-cas9 system is a viable, efficacious, and more cost-effective treatment option than current treatment regimens for HIV

METHODS

Search terms: CRISPR-Cas9, HIV, cure, and treatment were used to locate relevant articles.
Databases: Academic Search Complete, MEDLINE, and Consumer health complete.
Inclusion Criteria: The original preferred inclusion material consisted of U.S.-based research and both males and females of any age. However, CRISPR-Cas9 as treatment for HIV has not been trialed on humans at this time, and therefore, the search expanded to include animal trials and trials in human-derived cells.
Exclusion Criteria: Articles older than 10 years old and non-English articles

RESULTS

- In regards to a target site, it seems that the most effective solution is to target multiple areas, including the LTR-promoter so that viral escape is prohibited.[6,7,8]
- For administration of CRISPR into the human genome, studies have included adeno-associated virus (AAV) vectors, lentiviruses, nanoparticles, or cellular exosomes. Although adeno-associated viruses and lentiviruses have been studied most extensively, it seems that nanoparticles or cellular exosomes may be necessary in order to access a larger number of infected cells.[9]
- The main safety concern with CRISPR-Cas9 is the possibility for off-target cleavage, which could induce important gene mutations and chromosomal translocations, but since initial development, many efforts have been made to reduce-these effects in the standard CRISPR-Cas9 system.[10] In addition, direct delivery of Cas9 ribonucleoproteins (RNPs) rather than use of viral vectors will decrease off-target effects in that the RNPs will be degraded after editing the target DNA.[11]
- Cost is the most variable factor associated with CRISPR-Cas9 as therapy for HIV.[12] While inexpensive to design, developers of the drug will have the ability to inflate prices as desired.[13] However, it can be assumed that insurance will cover this therapy as it has done with other novel therapies in the past, but this is not definite and still poses as a problem for the uninsured.[13]

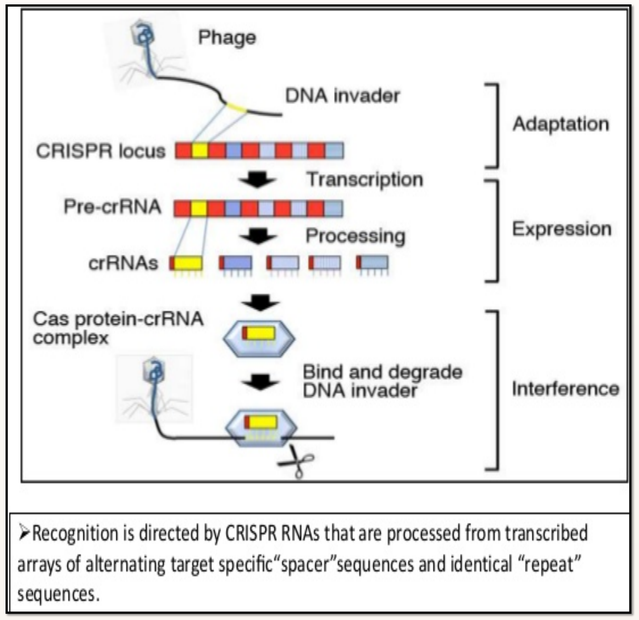

Figure 1. CRISPR-Cas9 immune mechanism: spacers and repeat sequences

CONCLUSIONS

Overall, the idea of CRISPR-Cas9 as treatment for HIV in humans is still very new, but current studies indicate that it may hold promise as a safe and efficacious treatment for HIV patients. Researchers are making great strides in overcoming uncertainties about an HIV target site, administration, and cost. If research continues to progress at this pace, the gene-editing system has the potential to cure infected patients of HIV, thereby improving their quality of life by eliminating complications related to diseases and potentially reducing their financial burden assuming the cost is lower than HAART therapy. Furthermore, not only could CRISPR-Cas9 benefit those with HIV in this instance, but also society as a whole by eventually eliminating the current epidemic as more people reach a cure. Ultimately though, more research must be done before CRISPR-Cas9 can definitively be called an appropriate treatment for HIV-infected individuals.

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