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On Novel Anti-viral HIV Gene Editing Platforms

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Editorial

Developing a new drug entity from drafting its structure to market launching is a complex process which can take many years and cost millions of dollars. It may also take many years to grow an idea of supporting evidence before selecting a pharmacological target for a costly drug discovery programme. This reflects a massive investment in terms of time, money, human and other potential resources. Only for the human immunodeficiency virus (HIV) vaccine, scientists have been working over 30 years and it is estimated that $500 million is being spent every year over the last decade on a candidate HIV vaccine [1]. Creating an effective drug against HIV represents one of the greatest biological challenges of a generation. Despite the new entry vaccines in clinical trials and the medical achievements, the fight against the fatal global epidemic virus continues. However, the scientific community has failed to address the scourge of HIV beyond the use of some drugs to control the HIV infection and to reduce viral load. The use of hitherto classical techniques had no promising results since the life expectancy of the HIV patients is very short in many cases. The landscape of HIV treatment must be changed dramatically and new horizons should arise including new strategies for the fight against HIV in the future.

Novel genetic engineering technologies have been developed enabling precise editing of genomes and these have numerous important clinical applications including the treatment of genetic diseases, viral infections, and Cancer. These new classes of reagents can specifically target nucleotide sequences within the cellular genome. The ability to correct gene associated mutations is an attractive approach as a treatment option. Based on recent studies, the *CRISPR/Cas9* gene editing system has been used to target the HIV-1 long terminal repeat (LTR) of integrated pro-viral DNA in the genome of cell in tissue culture and was able to inactivate viral gene expression and replication in a variety of latently infected cells [2]. This is an important first step in a potentially promising approach towards a new therapeutic pipeline that aims to eliminate all the permanently integrated DNA proviral copies of HIV-1 in an infected individual. It can also be used as a measure of the efficacy of *CRISPR/Cas9* in cells to which it is delivered, independent to cell type.

The idea of target HIV pro-viral DNA using uniquely tailored gene editing technology will open new horizons for more accurate and efficient elimination of different types of HIV. Furthermore, this way of HIV therapy is much more biocompatible to the human organism with fewer side effects than the already applied techniques considering that site-specific editing of DNA in human cells by co-expressed *Cas9* endonuclease from Streptococcus pyogenes and a short guide RNA (gRNA), is a biological process that can be mediated in human organism by the gene editing system and cell's own DNA repair machinery. Although the idea of targeting HIV-1 proviral DNA using uniquely tailored gene editing technology has been reported a few years ago and has counted some important attempts, it still is in a primary level and needs more exploration in several fields including new specific targets in the HIV proviral genome that flank the provirus and allow complete excision of the integrated provirus. In a recent study, Khalili present how the specialized innovative technology of tailored gene editing is applied to HIV retroviral nucleotide sequences using advanced methods and novel *in silico* techniques. The study aims to identify sequence specific conserved patterns suitable for gene editing-based HIV targets such as long terminal repeat (LTR) and tandem repeats polymorphisms (TRP) [3].

One of the obstacles to analyse of the HIV is its high genetic variability. The viral genome amount of the different forms of HIV is increasingly growing with the use of high-throughput DNA sequencing technologies. One of the major goals is to align, cluster and analyze the viral genomes of the different forms of HIV. Many issues must be addressed including the massive amount of data, the multiple sequence alignments based on homolog blocks, the hybrid sequence alignments, the classification of different HIV strains in clusters, the statistical analysis of genetic variations, the conserved motifs and patterns exploration and the nuclear genome comparisons between HIV infected and non-HIV infected cells. Therefore, fast, flexible and memory efficient bioinformatics techniques will be performed to facilitate analysis of thousands of samples simultaneously. New sequence specific HIV patterns can be identified from the successful execution of the proposed genome-wide scale computational analysis. Furthermore, significant insights about the HIV duplicative stepwise viral evolution will be provided. Therefore, collecting and separating the different forms of HIV in groups will increase the likelihood of finding the most representative sequence specific conserved motifs for gene editing-based HIV targets and eventually will lead to a powerful and effective treatment against HIV.

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