Analysis of HIV Cure

HIV is world wide issue that effects millions of people. This virus has proved to be very hard to combat against due to the nature of how it reproduces. Since the discovery of the virus it has shown to be very deadly disease taking millions of lives. Research to find a cure for this virus has been proven at this point to be extremely complicated. When researchers find a possible breakthrough it always seems varied amount issues arise out of it, making a barrier for finding a cure. This is a review on the history of the virus, the breakthroughs and what is next to finding what seems to be an elusive cure.

Background

An area that has been most effected by HIV/AIDS is Sub-Saharan Africa. This mostly because this where the disease first originated. It was first recognized as a human disease in 1981 after reports of homosexual men contracting a virus that had traits not seen before. It was soon recognized as a retrovirus that spreads though mucosal surfaces. The origin of the disease is said to be by a consequence of cross-species infections. Since its discovery the infection has infected around 60 million people and has killed more than 25 million people (Wang et el. 2016).

HIV/AIDS is the leading cause of death in Sub-Sahara Africa (Wang et al. 2016). With the introduction of antiretroviral therapy in 1996 the amount of deaths caused by HIV/AIDS decreased tremendously (Granich et al. 2015). Many programs would soon be created to help research and raise awareness of the virus. It would prove to be expensive costing the United States nearly 10 billion dollars (Wang et al. 2016).

Prevention Efforts

A cure for the virus has not been found but there are methods to either prevent the spread or prolong the life of those with HIV. People who fall in high-risk groups to contract the virus can reduce the chances of getting it. Studies have shown by using a pre-exposure prophylaxis called microbicides can get up to 86% reduction of possibility of getting the virus. Pre-exposure prophylaxis like microbicides have now been the main recommendation for prevention by the World Health Organization (WHO) (Vamvaka et al. 2018). Microbicides are used by applying to vaginal or rectal mucosal surfaces which helps prevent the person from receiving the virus (Mcgowan 2006). Microbicide works by acting like a barrier for the mucosal surfaces. It inactivates or blocks the pathogens before it can enter and infect the person (Naswa et al. 2012).

Another form of pre-exposure prophylaxis that is used is circumcision. Male circumcision can provide 60% protection from acquiring HIV. This procedure is a popular method for HIV prevention in Sub-Saharan Africa (Davis et al. 2018). The inner foreskin lacks protective tissue like keratin and contains cells that HIV can target. After contact with infected partner infected, T-cells from the latter form viral synapses with keratinocytes and transfer HIV to Langerhans cells via dendrites that extend to just under the surface of the inner foreskin. Langerhans cells then migrate the HIV virus to the basal membrane where it can then infect T-cells to reproduce (Morris and Wamai 2018).

Shock and kill

One of the big issues for finding a cure for HIV is the ability for it to stay undetected. HIV patients can have infected cells that contain the virus, but it is latent meaning that it is not reproducing. The virus still holds the capability to reproduce however. For the antiretroviral therapy to work the virus cannot be latent (Clutton and Jones 2018). Latency reversal agents can be introduced and cause the HIV to start reproducing again (Archin et al. 2012). However, latency reversal agents did not show signs of decreasing latent cells. This concluded that the bodies immune system must be involved in targeting these latent cells. This lead to the method called “shock and kill” or “latency reversal and clearance” (Clutton and Jones 2018).

However, this method would also show to have complications. One of the biggest issues that researchers run into is finding the number of cells that are infected with HIV. Most of the methods that are used to find the number of HIV-infected cells are PCR-based, quantifying total or integrated HIV DNA or RNA transcripts. This method concluded that there is overestimate the number of cells infected (Battivelli et al. 2018).

This would later be determined to be false and incorrectly estimates the number of cells in infected. There is possibility that the amount infected cells are way more than first thought to be. If that’s the case, then that means the amount of cells that impacted by latency reversal agents is much less then thought to be at first (Battivelli et al. 2018). More specifically, the heterogeneous nature of HIV latency and suggest that HIV reactivation is a stochastic process that only reactivates a small fraction of latent viruses at any given time (Chen et al 2016). This does not exactly make the idea of using “shock and kill” method obsolete but instead steers research in a possibly new direction.

Genetic Approach

“Shock and kill” method seem to be the most popular research topic among scientistist when it comes to finding a cure for HIV. There is another approach that has been explored and that is

dealing with the genetics of the virus. Some of the ideas includes removing the proviral HIV-1 genome from host cell DNA, by targeting its highly-conserved 5' and 3' long terminal repeats. Disrupting HIV-1 entry coreceptors (CCR5, CXCR4) and proviral DNA-encoding viral proteins. Engineering resistant cells by prior immunization. Selectively deleting HIV proviral DNA integrated into the host genome. Targeting specific cis-acting elements within the long terminal repeats (Wigdahl 2014).

CCR5 gene seems to be a gene that peeks the interest of many scientist. CCR5 is a gene that codes for chemokine receptors which are found on cell surfaces and promote cellular migration by chemotaxis. The chemokine receptor CCR5 helps to initiate immune responses and to distribute effector immune cells to sites of inflammation. CCR5 is also a key cellular receptor that is required for almost all instances of HIV infection (Lederman et al. 2006). Gene editing of CCR5 gene can lead to disruption of HIV ability to infect. However, it does seem that it will be sometime before this can be used as a possible medical procedure. One of the reasons being that delivery of gene-editing mediators have not been fully optimized. Another reason is that off target effects have not been explored when it comes to the entire genome (Manjunath et al. 2013).

Future

The goal of HIV research is to find a cure for it. This means that the viral reservoir must be eradicated. However, at this point finding a cure might be far off because no treatment has been discovered that would fully eradicate the viral reservoir. Treatment to prolong the life person with the virus is the global approach. Early detection and treatment are very important and at this point is the best way to fight the virus (Passaes et al. 2014). There does seem to multiple approaches to finding a cure. This is by using latency-reversing agents to activate the viral reservoirs, immunotherapies including innate immunity activators and effector antibodies, gene therapies, and therapeutic vaccines to eliminate the persistent viral reservoirs or induce effective immune control of HIV infection (Cihlar and Fordyce 2016). All these methods show some promise but are far off from being used as a form of treatment. One of the problems is that immune response to these treatments are not well understood (Passaes et al. 2014). Another problem is that clinical trails have not been tested enough to show if investment in these procedures are worth it (Lewin and Rouzioux 2011)

Conclusion

Since the discovery of the virus in 1986 there has been massive breakthroughs for HIV treatment. In 1996 antiretroviral treatments started to be administered and since then has saved millions of lives. Before HIV was pretty much an automatic death sentence. At this point the best

way to deal with HIV is prevention. That is finding ways to prevent the virus from spreading. These methods include circumcision and microbicides. However, what many researchers are aiming for is the complete eradication of the virus. Something that can destroy the virus and prevent possible infection from happening again. This has been extremely difficult to find but some promising methods have been found like the use of the “shock and kill” and gene editing. These methods are in the beginning stages and it may be a long time until it can be used besides in trails. Research into these methods and ones like this must continue.