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Genes and Genome of HIV-1

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Abstract

There are currently various different tests for HIV infections such as HIV antibody test, P24 antigen test, Polymerase chain reaction test (PCR), Fourth generation test and Home test. Even though there is no particular treatment or therapy for HIV, very effective treatment called antiviral therapy, combination therapy, or HAART (highly active antiretroviral therapy) can retain the virus under control and permit someone with HIV to have an active, health life. Some people have acquired the side effects from their medications, such as nausea, diarrhoea, prolonged headaches, depression and mental health problems. Emergency anti-HIV medication (PEP) may stop people becoming infected, but treatment must be started within three days of coming into contact with the virus. HIV symptoms have not appeared in many of the people. Blood test is the only way to find HIV infection. We can reduce the HIV infection by using a condom during sex and reducing the number of partners. HIV regulatory, accessory proteins and envelope proteins are play a major role in vaccine development. Anti-HIV vaccines have required generating neutralizing antibodies (NAbs) and effective T-cell responses. Recently FDA has approved the one vaccine SAV001 for human clinical trial that is very important milestone for vaccine development. This vaccine has the potential to save the lives of people by preventing HIV infection.

Keywords: HIV infections;HIV-1; HIV-2

Introduction

Based on the geographical origin and organization of genome HIV-1 and HIV-2 are differentiated in the worldwide. The HIV-1 is predominantly common virus in the worldwide than HIV-2. HIV-2 has identified in West Africa region and rarely identified in other places. The majority of the people in America, Europe, Asia and Australia have infected with subtype B of M group HIV-1 virus. The subtypes A, C and D have concentrated in Africa region [1].

The genomic length of HIV is around 9.5 kb. Researchers have categorized the HIV-1 virus into groups, subtypes and sub-subtypes that classification is based on the genetic variation and phylogenetic analysis. The HIV-1 is divided into three groups like M, N and O group. M group of HIV-1 is further divided into subtypes as A-D, F-H, J and K subtype. The present global epidemic has occurred by M group viruses other than N and O group viruses. In South America most people have infected with HIV by the reason of injecting drugs and homosexual. The HIV genetic subtypes, such as B subtype, BF recombinants and F subtype are most responsible for HIV infection. In Argentina most people have infected with CRF12_BF recombinant forms HIV subtypes. CRF defined as circulating recombinant forms [2].

Based on the genome organization and phylogenetic relationships, clinical characteristics, virulence, infectivity and geographic distribution, HIV-1 and HIV-2 both species are differentiated. According to the serological evidence in the beginning of the HIV-1 epidemic, African green monkeys are used as carriers of an HIV-1-like virus and simian T-cell lymphotrophic virus 3 (STLV-3, now Simian Immunodeficiency Virus (SIV)). Based on the cross-species transmission researchers have believed that HIV-1 jumped to humans from African green monkeys. According to the phylogenetic evidence, numerous cross-species transmission events occurred between chimpanzee (*Pan troglodytes troglodytes*) SIV (SIVcpz) and sooty mangabey SIV (SIV sm) with humans to produce the HIV-1 and HIV-2 strains. Most of the lentiviruses are identified in more than 40 species of African primates [3].

According to the Oral Polio Vaccine (OPV) hypothesis, in 1960, HIV was introduced into human populations by the use of polio vaccine which was produced from African green monkeys. TMRCA method is used to know the common ancestor of HIV-1; it may be present in human or a chimpanzee host. TMRCA defined as the time to the most recent common ancestor (TMRCA) of HIV-1 and by using these method scientists expected that M group of HIV-1 has originated proximate in the 1930 [3].

According to the archival samples such as DRC60 and ZR59, in the 1960 genetic diversity of HIV-1 has occurred in West Africa. The new HIV-1 group p has identified in Cameroonian woman. Group P play a key role in human–gorilla transmissions hypothesis. In phylogenetic analysis group p situated as the sister taxon to all SIVgor. But it is situated separate from HIV-1 group O [3].

In the US in 1981 the first cases of acquired immunodeficiency syndrome (AIDS) were labelled in homosexual men. Retrovirus (HIV) was causative agent for AIDS, confirmed by French and American scientists in 1983 and 1984. According to the records around 25 million individuals were died from AIDS and above 33 million people have infected with HIV. In 2007, 2 million people have died with HIV and 2.7 million people have newly infected with HIV. The International AIDS Society's XVII have conducted a conference in Mexico City to discuss regarding HIV infection, prophylactic HIV-vaccines, topical antiviral microbicides and antiviral treatment [4].

In this report, I have discussed about HIV structure, genes and genome, Phylogenetic relationship, natural infection, epigenetic modification, apoptosis, Anti-retroviral therapy and vaccine development.

HIV-1 structure

HIV, of the genus *Lentivirus*, is a *retrovirus*. Retroviruses are enveloped viruses. HIV contains two identical, single stranded RNA molecules as a genetic material in the center. It is enclosed by viral nucleocapsid (NC) protein, or p24. There are some in the virus layer

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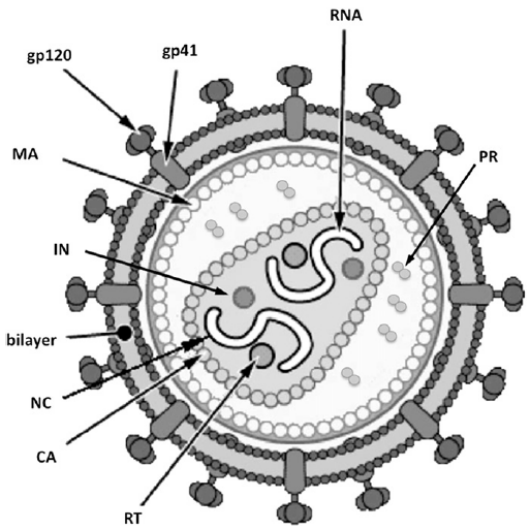

Figure 1: Diagram of HIV-1 mature virion..

Figure 1 NC represents the Nucleocapsid, CA represents the Capsid and RT represents the Reverse transcriptase, IN represents the Integrase, PR represents the Protease, MA represents the Matrix protein

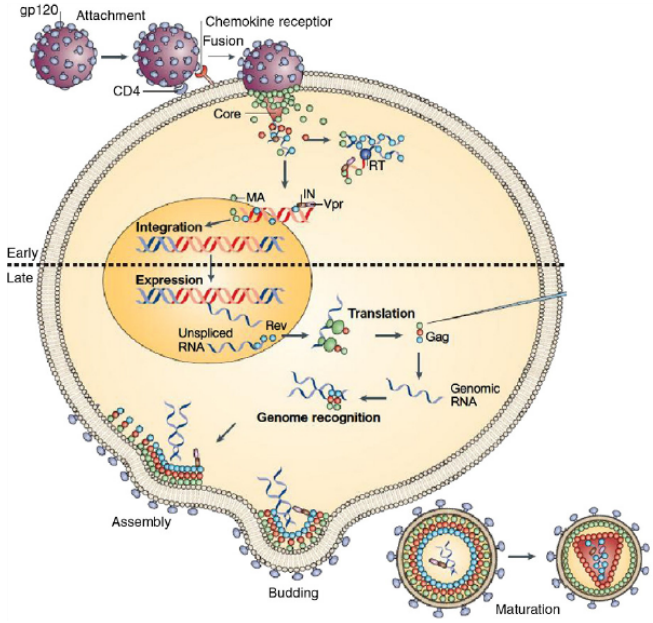

Figure 2: Overview of HIV-1 life cycle.

Figure 2 shows the life cycle of HIV-1. i the life cycle figure we can observe the central dogma of life that is replication, tranascription and translation.

and typically 7 internal proteins, 4 of which are structural and 3 enzymatic. The three enzymatic proteins reverse transcriptase (RT), integrase (IN), protease (PR) is surrounded by structural protein and matrix (MA) protein, or p17.The HIV structure consists of lipoprotein surface studded by envelope knobs consisting of the glycoproteins gp120 and gp41 [1].

HIV-1 Life cycle

A retrovirus may become a Human Immunodeficiency virus-1 enters by fusion between attachment spikes like viral glycoprotein gp 120 (Surface envelope protein), gp41 (Trans membrane protein) and the host cell receptors (CD4, chemokine). Uncoating release the two viral RNA genomes and the viral enzymes (Pol proteins) reverse transcriptase (RT), integrase (IN) and protease (PR). Reverse transcriptase copies viral RNA to produce double stranded DNA. The new viral DNA is transported into the host cell's nucleus, where it is integrated into a host cell chromosome as a provirus by viral integrase (IN).The provirus may be replicated when the host cell replicates. The transcription of the provirus may also occurs, producing RNA for new retrovirus genomes and RNA that encodes the retrovirus capsid (CA), enzymes, and envelope protein. Viral proteins are processed by viral proteases: some of the viral proteins are moved to the host plasma membrane. Mature retroviruses leave the host cell, acquiring an envelope and attachment spikes as it buds out. Provirus that replicates in latent state and it may produce new retroviruses [5].

CCR5 and CXCR4 are seven transmembrane G protein-coupled chemokine receptors that act as coreceptors for HIV-1entry [6].

The above figure shows the developmental process of HIV particles between the cellular process and villi. Arrow sign indicate the mature virion cone shaped cores. The double arrows indicate the intermediate state in maturation. The budding viruses are shown by arrow heads. The other particles shown the immature virions released by the cell [7].

Genes and Genomes

In the late phase of viral replication similar to all retroviruses, the human immunodeficiency virus selectively packages two copies of its positive strand, unspliced, 5′-capped, and 3′-polyadenylated RNA genome. The retroviral Gag proteins are involved in packaging of the genome. In the direction of N terminal to C terminus the Gag protein has three individually folded domains such as matrix (MA), capsid (CA), and nucleocapsid (NC) and three other unstructured segments. In the Genome selection process the NC binding to the ψ sites of conserved RNA. This ψ sites are normally situated close the 5′-end of the viral RNA. The ribonucleoprotein complex is trafficked to

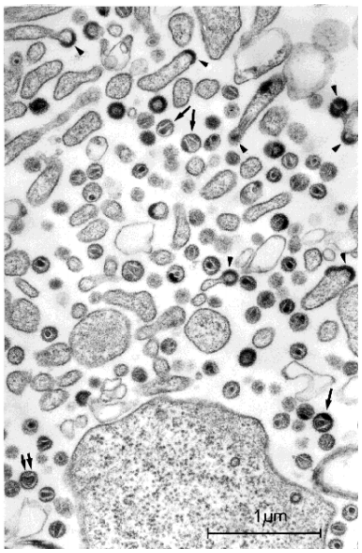

Figure 3: Thin section EM of HIV-1 strain IIIB.

The above figure 3 shows the developmental process of HIV particles between the cellular process and villi. Arrow sign indicate the mature virion cone shaped cores.

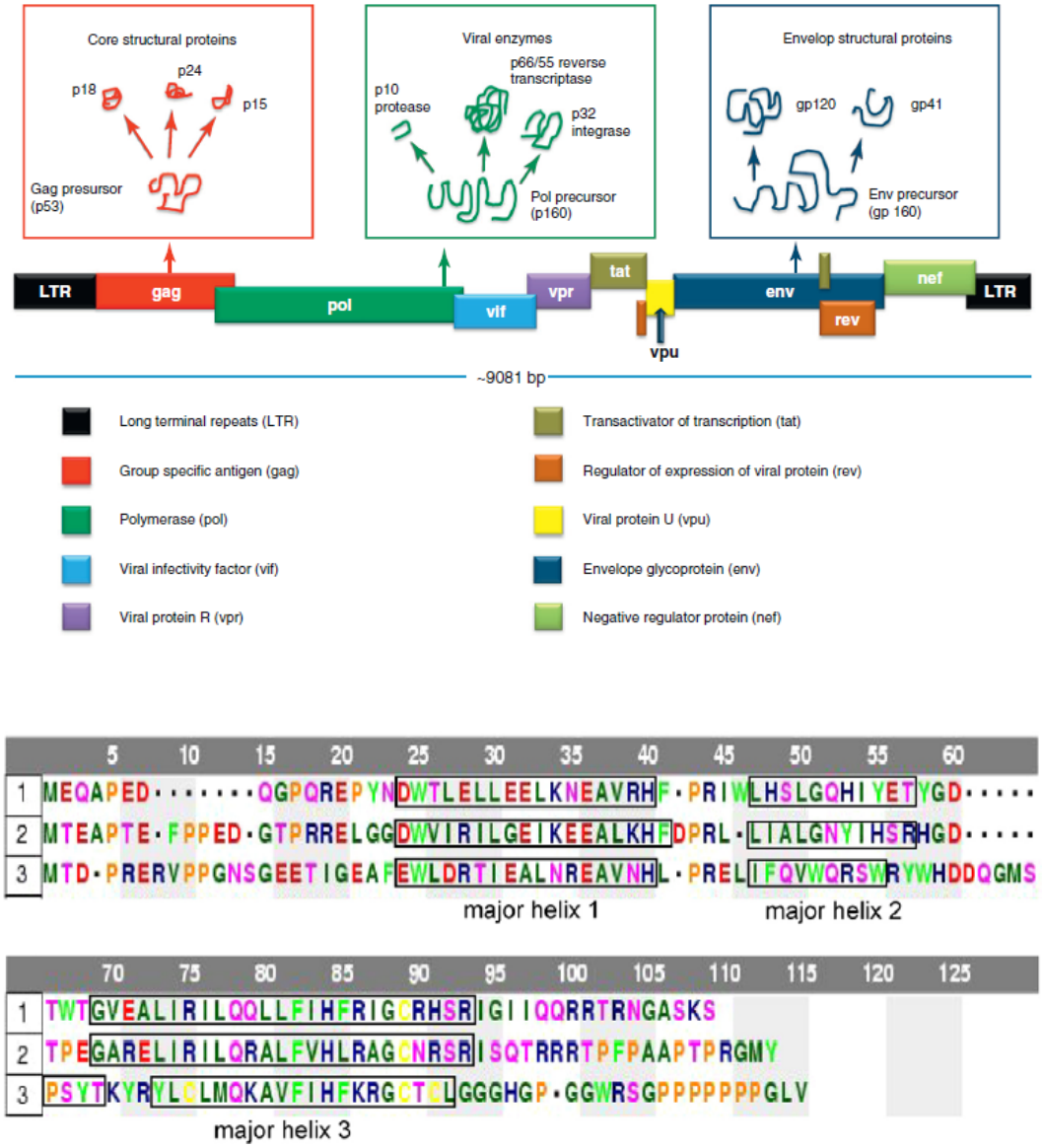

Figure 4: Sequence alignment of Vpr/Vpx proteins.

lipid raft assembly sites on the PM where a number of Gag molecules localize and assemble to form an immature virus particle. After the budding process the mature and infectious virus particles are formed by cleavage of the Gag proteins with viral protease. The infectious virus particles are formed by the rearrange of mature MA, CA, and NC proteins which are produced from the cleavage of Gag proteins. During reverse transcription, the two RNA molecules are used for strand-transfer-mediated recombination which leads to production one DNA allele. Therefore retroviruses are considered as pseudodiploid. This recombination process is used for viruses to increase the fitness in many ways like a defence against restriction nucleases [8].

Virus structural Pr55 gag, and Pr155 Gag-Pol precursure protiens combine with genomic RNA to form the virus at the plasma membrane. The gag gene is codes for a precursor polyprotein(Pr55) that is cleaved by viral protease(PR) to make 4 smaller internal structural proteins of mature virion: 1) Membrane associated or matrix protein (p17), 2) capsid protein (p24CA), 3) Nucleocapsid (p10 NC) ,4) C-terminal core-envelope link (CEL, p6L1). The protease has coded by pol, and it is part of a second long ploy protein (Pr160) produced from a gag-polRNA. The viral Pr160 Env precursor is cut into two smaller glycoprotein molecule (gp120 and gp 41) by ahost cell protease as the virus particles bud from the cell membrane. Gp 120 is surface protein (SU) and Gp 41 is transmembrane protein (TM) figure 4 [7].

Based on the angular shapes of SIV and HIV, these were denoted as isometric, icosahedral structures. Highly basic region of the N-terminal MA domain and co-trnslational myristoylational are necessary for MA to binding with plasma-membrane which leads the formation of infectious HIV. The binding of phospholipids with these factors are useful for MA to perform the function. The self association of Gag and Gag–pol ploy proteins need the matrix proteins. The C and N terminal regions of p24 CA required for the formation of the RNP shell and cone–shaped core. Major homology motif is situated at the middle region of the CA which is essential for the formation of infectious virion. At the viral maturation stage time 14 aminoacid

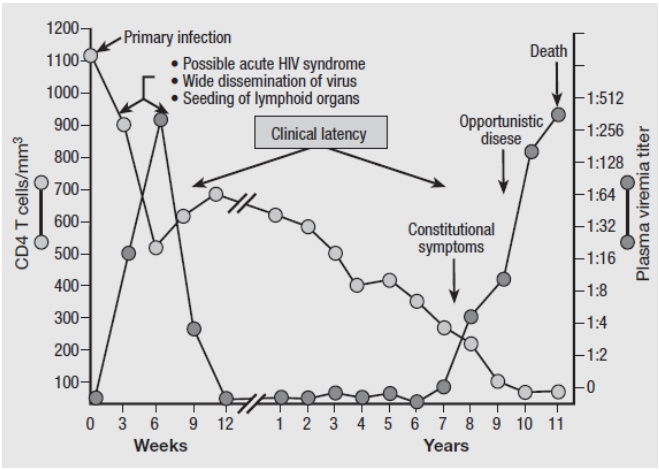

Figure 5: History of HIV infection without therapy .

Capital I in this figure 5 number protein alignment, 2 number inicates the HIV-2 Vpr protein alignment, 3 indicates the HIV-2 Vpx protein alignment.

- Number 1 indicates the HIV-1 Vpr protein alignment
- Number 2 inicates the HIV-2 Vpr protein alignment
- Number 3 indicates the HIV-2 Vpx protein alignment
- Boxes indicates the Helices of proteins

spacer p2 detached from the C-terminus of p25 CA. It is situated between CA and NC. The spacer p1 situated between NC and p6 CEL. At the time of encapsulation process the two zinc-finger-like motifs are useful for the interaction of NC domain with viral RNA. In compare to the other retroviruses; lentiviruses (HIV-1) have an additional P6 domain. P6 is needed for viral budding process. It is derived from the C-terminal portion of the Pr55 polyprotein. The viral enzymes reverse transcriptase (RT), integrase (IN), and protease (PR) are derived from the cleavage of Pr155 Gag-Pol. The accessory proteins; Vpr and Vpx are also present in the core with same amount of Gag. The Vpx is appeared only in the HIV-2 and SIV, but Vpr is present in the all lentiviruses. The virion contains structural and accessory proteins including with host cell proteins for example actin, ubiquitin, and cyclophilin [7].

HIV subfamily and HTLV 12 genomes are varied in the nucleotide composition .HIV contain high amount of adenine, low amount of cytosine and low amount compared to HTLV 12. In supplement, CpG dinucleotide are high in HTLV12 than HIV. These two properties are utilised to direct integration of the retroviral genomes into exact segments of the human chromosomes [9].

Structure and cytopathogenic activity of HIV Vpr/Vpx proteins and genes

The vpx and vpr genes are presented in the HIV-2 and SIVs which is isolated from rhesus (SIVmac) and sooty mangabey (SIVsm) monkeys. According to the latest report these both genes are also present in the SIVs from the mandrill (SIVmnd-2), red-capped mangabey monkey (SIVrcm) and drill (SIVdrl) like HIV-2 group. In rhesus monkeys AIDS has initiated by vpr and vpx genes of SIVmac. The vpr and vpx genes are translated into 100 amino acids of small proteins. The HIV-1 Vpr has three major α-helices surrounded by N and C-terminal loops which have determined by NMR. The HIV-1 Vpr and HIV-2 Vpr have shown cytopathogenic activity like cell cycle arrest at the G2 phase while Vpx of the HIV-2 did not display this activity. HIV-1Vpr has shown apoptosis activity while the role of Vpr/Vpx of the HIV-2 group in the apoptosis still not understood. The structures of the HIV-1Vpr and HIV-2 Vpr/Vpx are somewhat similar, but have dissimilar characteristics. HIV-1 Vpr and HIV-2 Vpr/Vpx are detrimental to target cells. Multiple sequence alignment or ClustalW program has used to compare the structural similarity of the HIV-1 Vpr and HIV-2 Vpr/Vpx proteins. The three proteins have three major amphipathic ∞helices which surrounded by N- and C-terminal loops. According to the Sequence homologies, the sequence of HIV-2 Vpx is somewhat different from HIV-2 Vpr and HIV-1Vpr. In a major helix 2, between 2 and 3 helices HIV-2 Vpx has lower sequence identities with HIV-1 Vpr and HIV-2 Vpr proteins. In the region between 56 to 72 amino acids HIV-2 Vpx has both a-helix and a long loop. Tyrosine amino acids (68, 71 and 73) are present adjacent to the Vpx which leads to the virion assimilation. HIV-2Vpx contain several glycine's (93–105) in the first half of the C-terminal loop while the two Vpr (95–104) have hydrophilic amino acids and arginine's. These arginine's (100 and 101)are useful for cell cycle arrest at G2 phase in the HIV-1 Vpr. Vpr/Vpx of HIV-2 have a long N-terminal loop and bunched prolines in the second half of the C-terminal while HIV-1Vpr does not [10].

HIV Natural infection

HIV is transmitted by sexual contact, blood transfusion, blood semen, vaginal secretion and breast milk [1].

Parental route and sexual contact are major factors for transmittance of HIV. In the first step, HIV is transported to lymphnodes for binding and it replicates and induces permanent infection at the lymphnodes. In the last few years it has been verified that in the gastrointestinal tract. $CCR5^{+}CD4^{+}$memory T lymphocytes have targeted by HIV in the early phases of infection. This leads many destructive events such as destruction of CD4 cells, break of intestinal mucosa, microbial translocation products are entered into the systemic circulation and all body parts are infected. In the primary HIV infection, symptoms like consisting in fever, malaise, generalised Lymphadenopathy, pharyngitis, diarrhoea and rash are rarely predictable because these symptoms are non-specific. HIV transmitting infection is increased by the increase of Plasma HIV RNA levels. When CD4 cell count drops to lower than 350 cells/mmc, it leads to several AIDS- or non AIDS-associated events (infections or tumors). We cannot escape from death in the absence of treatment. Some patients are able to control the infection by maintaining low viremia and high CD4 cell count even in the lack of therapy. These patients are called as elite controllers because they have natural resistance to HIV infection. The HIV infection is reduced by using antiretroviral therapy, but it is not entirely eliminate the HIV infection figure 6 [11].

The figure 6 shows that HIV-1 is closely related to the SIVcpz (chimpanzees virus) and HIV-2 is closely related to the SIVsm (sooty mangabeys virus), but HIV-1 and HIV-2 are not adjacent to each other. On the basis of phylogenetic relationship we can conclude that M,N,O groups of HIV-1 are significantly more closely related to the SIVcpz strains(*P.t.troglodytes*) than SIVcpzAnt *(P.t.schweinfurthii*) from West Central chimpanzees, the cross-species transmissions giving rise to HIV-1 most probably all occurred in West equatorial Africa. M group of the HIV-1 shows greatest diversity in the region of west equatorial Africa [13].

Epigenetic modifications

Epigenetics are the study of heritable changes in gene function that occur without a change in the DNA sequence. Epigenetic regulators include DNA methylation, histone modifications such acetylation, phosphorylation, and methylation and RNA associated silencing influence the integration and latency of HIV-1 cycle by gene regulation.

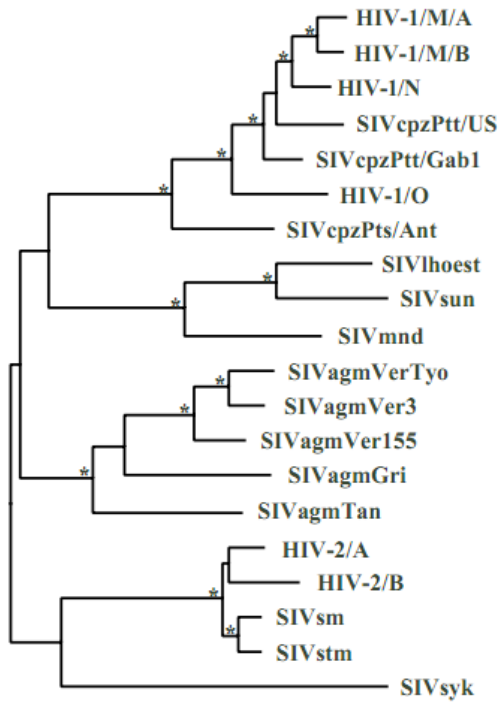

Figure 6: Evolutionary relationships among primate lentiviruses.

Figure 6 shows that HIV-1 is closely related to the SIVcpz (chimpanzees virus) and HIV-2 is closely related to the SIVsm (sooty mangabeys virus), but HIV-1 and HIV-2 are not adjacent to each other.

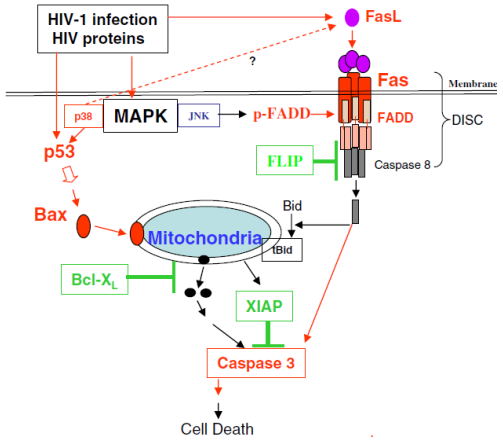

Figure 7: Association of HIV-1-induced cell death pathways with HIV-1 replication.

Red colour indicates increase of HIV-1 replication.Green colour indicates inhibition of HIV-1 replication. Black colour indicates no test or no effect on HIV-1 replication [14].

The epigenetic modifications include H3 acetylation, H4 acetylation, and H3 K4 methylation support the HIV-1 integration which is inhibited by H3 K27 tri methylation and DNA CpG methylation. In Murine Leukemia Virus the integration process is favoured by CpG islands. Formerly, Coffin et al. [12] have informed that CpG methylation in Avian Leukosisvirus favour the integration process [5].

Moreover, yeast retro transposons bind to the methylated histone tails by chromo domains and these retro transposons encoded the integrase enzymes. The provirus genome has inactivated by CpG methylation at transcription level. This latent provirus is reactivated by 5-Azacytidine (5-AzaC) which induces the demethylation. The promoter activity of the HIV-1 supressed by DNA methylation. Transcriptional regulation of host factors like lens epithelium-derived growth factor (LEDGF/p75) increased the integration by binding to HIV-1 IN. RNA interference technique is used to weaken the HIV-1 integration by supress the LEDGF/p75 expression. Drugs such as amphetamines, cocaine, marijuana, and opiates serve as cofactors for regulate gene expression inCD4$^+$ lymphocytes via epigenetic modifications the chromatin structure of CD4$^+$ T lymphocytes under take wide changes via epigenetic modifications during cytokine production [5].

Apoptosis

HIV-1 promote the apoptosis by direct killing the CD4-expressing infected cells, such as CD4$^+$ T helper, T lymphocytes and dendritic cells .Apoptosis is occur by two pathways an extrinsic (death receptor-mediated, such as Fas/Fas ligand) and an intrinsic (Bax/mitochondrial mediated) pathway. Fas ligand on the surface of a killer lymphocyte activates Fas death receptors on the surface of the target cell. The cytosolic tail of Fas then recruits the adaptor protein FADD via death domain on each protein. Each FADD protein then recruits an initiator procaspase-8 via a death effector domain on both FADD and the procaspase, forming a DISC. Activated Caspase-8 then activates Caspase-3 in Jurkat cells which leads to the apoptosis. Association of certain Bcl-2 proteins with the mitochondrion causes it to release

Cytochrome c from the intermembrane space into the cytosol. The cytochrome c combine with Apaf-1 which leads to the formation of an apoptosome complex and then activates the Caspase 8, Caspase 3 which results cell death figure 7 [14].

Inhibition of HIV infection with highly active antiretroviral therapy (HAART)

Up to 2010 above 20 antiretroviral agents have used to treat HIV infection. These antiretroviral agents have received the license by based on clinical value and effect on plasma HIV RNA concentration figure 8

Human immunodeficiency virus (HIV) infection has treated by more than 25 antiretroviral drugs. The nucleoside and nucleotide inhibitors such as zidovudine, didanosine, zalcitabine etc., have used to block reverse transcription step by inhibiting reverse transcriptase (RT) activity. Viral protease is inhibited by saquinavir, ritonavir, indinavir etc. The most of the antiviral drugs have used to target the HIV-1 reverse transcriptase (RT) and the viral protease activities, but HIV-1 is highly variable and capable of increasing resistance to all of the antiretroviral drugs [6].

Based on the highly variable and resistance power of HIV-1, the new highly active antiretroviral therapy (HAART) has introduced to suppress viral replication to ground levels that means the drug resistance power of HIV-1 is prevented. HAART is the combinations of three or more antiretroviral agents. HAART is decrease the plasma viral load of HIV-1-infected individuals to untraceable levels, and then reduce disease development and Stimulates survival by improving CD4$^+$ T cell counts of individuals. HAART contain important disadvantages, such as metabolic, cardiovascular disorders, immune reconstitution disease and progression of resistant HIV-1 strains. Furthermore,

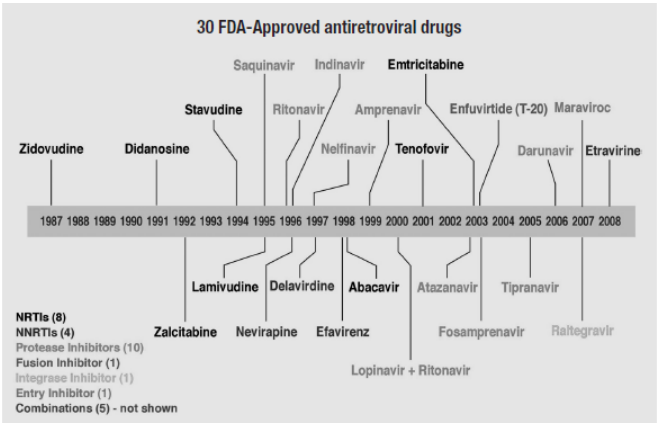

Figure 8: Approved antiviral drugs to treat HIV infection.

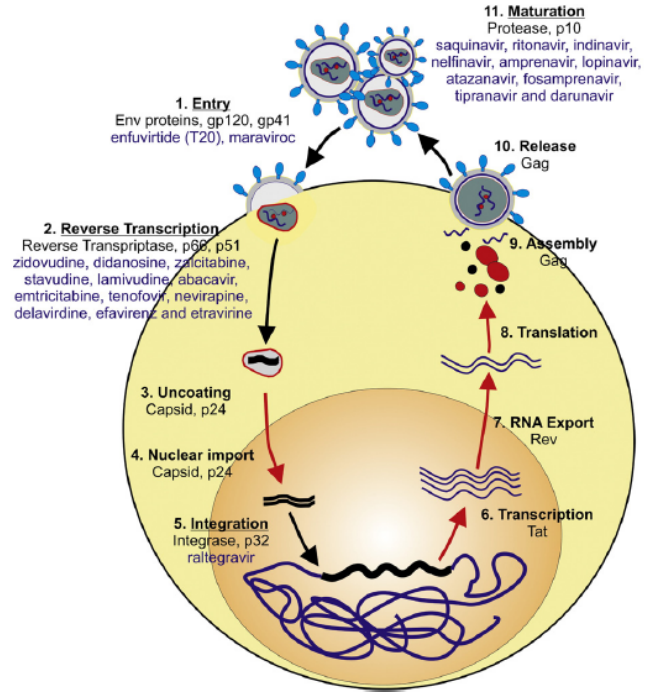

Figure 9: Viral replication cycle and the steps currently inhibited by HAART.

In the above figure 9 blue colour words have represented the antiretroviral agents that are used to block the HIV replication cycle.

Block colour words have indicated the viral proteins that are involved in the individual steps of viral replication cycle.

HAART is incapable to remove resting long-lived cells containing integrated proviruses and thus it requires life-long daily treatment. The membrane fusion events necessary for viral entry is blocked by binding of Maraviroc drug to the HIV-1 entry cofactor CCR5 and blocks its interaction with the viral envelope gp120. CD4 antibody or TNX-355 has blocked the later step in the viral entry Process by interaction with gp41. The HIV-1 replication is restricted by three host restriction factor such as cytidine deaminases (e.g. APOBEC3G), tripartite motif 5-alpha (TRIM5α) proteins and tetherin. The lethal hypermutation of the viral genome has induced by the cellular apolipoprotein B mRNA-editing enzyme, catalytic polypeptide like3 (APOBEC3) cytidine deaminase that was first host gene recognized as an inhibitor of HIV-1 infection. This lethal hypermutation is caused by the absence of Vif; APOBEC3G is incorporated into the budding virions and introduce G-to-A substitutions in the HIV-1 genome in figure 9 [6].

The lethal hypermutation is blocked in the presence of accessory viral Vif protein because that binds to a Cullin5-based ubiquitin ligase complex and antagonizes APOBEC3G by proteasome-mediated degradation. The nascent mature viral particles release is inhibited by restriction factor tetherin. Tetherin is also called as BST-2, HM1.24 or CD317. TRIM5α proteins have used to block the incoming retroviral capsids and it may cause the accelerated uncoating by proteasomal degradation [6].

In the HIV-1 strains tetherin is antagonized by Vpu. SIVs strains are used multi-functional accessory Negative factor (Nef) proteins to antagonize the tetherin because these strains lack Vpu gene. HIV-2 and Ebola viruses have used the envelope Glycoproteins to antagonize tetherin. Interferon-alpha (IFNα) is used to induce the expression of tetherin [6].

HIV Vaccine

Anti-HIV vaccines have developed from potent immunogens that are required to generate neutralizing antibodies (NAbs) and effective T-cell responses. A vaccine is used to provide long-term protection in the future against the same or similar immunogenic organism by inducing an adaptive immune response upon administration. In vaccine development, envelope proteins are paly a key role because T-cell epitopes and NAb epitopes have situated on envelope proteins. Enzymatic addition of alpha-gal epitopes to the carbohydrate chains leads to increase the Immunogenicity of glycosylated gp120. According to the Vaccination studies, HIV-1 Tat protein has used to balance theTh1 and Th2 response. Gag protein play major role inviral assembly and maturation step of virus replication cycle and act as a potential HIV immunogenic. Nef expression is used to increase the viral replication and stimulates the survival of infected host cells [14].

HIV Vpr protein promotes major events in viral life cycle like nuclear localization of the HIV genome, rises viral transcription and apoptosis of infected host cells. The antiviral factor APOBEC3G has degraded by Vif which is required for viral replication. HIV regulatory and accessory proteins are playing a major role in vaccine development. For example, DNA vaccine consist the multiple accessory proteins: Vif, Vpu and Nef, which are used to cause a Th1 response. In most cases, HIV immunogens are carried by vectors like adenovirus (Ad) and modified vaccinia virus Ankara (MVA). Comparing to other vectors; Ad5 vectors have induced the more CD8+ T-cell response. In the various stages of clinical trials New York attenuated vaccinia virus (NYVAC) and Sendai virus have used as vectors for an HIV vaccine. Conney et al. revealed that combined vaccine regimen like vaccinia plus gp160 used as booster to induce the neutralizing antibodies (nAbs) and CD8+T-cell responses. Long- lasting T-cell responses have induced by an NYVAC-based vaccine. In humans, MVA, canarypox and fowlpox have used to induce the weak primary T-cell responses. DNA vaccine is used to induce a weak CD4+ T-cell response in humans. DNA vaccine has required the cytomegalovirus (CMV) promoter which is used to stimulate expression and bovine growth hormone polyadenylation signals that are used to terminate the transcripts. Liposomes and virus-like particles (VLPs) have used as vectors to carry immunogens. VLPs are safe to use as vectors for vaccine development because they do not contain genetic molecules of virus. VLPs have used as vectors to inhibit HIV entry into cells by inducing an immune response against CCR5 co-receptor [15].

Discussion and Conclusion

HIV virus infects and destroys the white blood cells known as T-helper cells or CD4 cells in the body. Generally CD4 cells have prevented the human body from infections. Without treatment we are unable to fight against HIV infection. The rare infections or cancer have developed with HIV. These all factors are leads to cause AIDS. Currently, in developing countries around 34 million people have infected with HIV-1, every year around 2.5 million new people have infected with HIV and 2 million people are died per every year in the world wide. Life expectancy of HIV/AIDS infected Zimbabwe people has drastically fallen to 34 years for women and 37 years for men. HIV is transmitted by sexual contact, blood transfusion, blood semen, vaginal secretion and breast milk. HIV is also transmitted through oral sex and from a mother to baby during pregnancy, birth or breastfeeding. HIV is not transmitted through saliva and casual contact such as kissing or sharing glasses. HIV is very delicate virus so does not live long external the body. The first few months after people become infected with HIV is called primary HIV infection, or acute HIV infection such as severe flu, fever, sore throat, rash, swollen glands, headache, ulcers in mouth. Early symptoms have started with in four weeks after the infection and these symptoms have appeared in the above 70 percent of people who are suffered with HIV infection. In advanced HIV infection illness related with Tuberculosis, Pneumonia and Cancer which are uncommon in people who have been taking anti-HIV medicines. There are currently various different tests for HIV infections such as HIV antibody test, P24 antigen test, Polymerase chain reaction test (PCR), Fourth generation test and Home test. Even though there is no particular treatment or therapy for HIV, very effective treatment called antiviral therapy, combination therapy, or HAART (highly active antiretroviral therapy) can retain the virus under control and permit someone with HIV to have an active, health life. Some people have acquired the side effects from their medications, such as nausea, diarrhoea, prolonged headaches, depression and mental health problems. Emergency anti-HIV medication (PEP) may stop people becoming infected, but treatment must be started within three days of coming into contact with the virus. HIV symptoms have not appeared in many of the people. Blood test is the only way to find HIV infection. We can reduce the HIV infection by using a condom during sex and reducing the number of partners. HIV regulatory, accessory proteins and envelope proteins are play a major role in vaccine development. Anti-HIV vaccines have required generating neutralizing antibodies (NAbs) and effective T-cell responses. Recently FDA has approved the one vaccine SAV001 for human clinical trial that is very important milestone for vaccine development. This vaccine has the potential to save the lives of people by preventing HIV infection.

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