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HIV Aids Types, Groups and Subtypes

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Abstract – The most modifying envelope protein is HIV (Env). In this research, we use profound mutational scanning to estimate the effect of all Env amino acid mutations on cell culture viral replication. Most of the mutations are selected for purification in our experiments, while a few locations are selected to enhance the reproduction of HIV in cell culture. We compare the actual frequencies of these amino acids in naturally occurring HIV sequences to our experimental estimates of each site's preference for each amino acid. Our measured amino acid tastes are mostly matched in natural sequences of amino acid frequencies. Our found biases, on the other side, are less in line with natural amino-acid frequencies at surface-exposed sites that are subject to stresses not present in our tests, such as antibody selection. We test the inherent mutational resistance of each Env site with our results. We show that epitopes of mostly neutralising antibodies are significantly less able to resist mutations, proving a widely held belief. Overall, our findings shed light on how internal functional limitations and external selection pressures shaped Env's evolution.

Keywords – HIV, HIV-1, Aids, Types, Groups and Subtypes, etc.

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INTRODUCTION

In sub-Saharan Africa, HIV was believed to originate in non-human primates and was introduced to humans late in the 19th or early in the 20th century. The first paper on a pattern of opportunistic AIDS infections was written in 1981. It is suspected that both HIV-1 and HIV-2 came from western Central Africa and transferred from non-humans to humans organisms (a phenomenon known as zoonosis). The SIVcpz, a simian immunodeficiency virus (SIV) that infects wild chimpanzees, is apparently the cause of HIV-1 in Southern Cameroon (HIV-1 descends from the SIVcpz endemic in the chimpanzee subspecies Pan troglodytes troglodytes). The nearest cousin of HIV-2 is SIV (smm), an old world monkey living in West Africa. sooty mangabey (Cercocebus atys aty's) (from southern Senegal to western Ivory Coast). New World monkeys including owl monkeys are HIV-1 immune, perhaps due to a genetic merger of two virus-resistance genes. HIV-1 is expected to be at least three times beyond the species barrier, resulting in three virus types, M, N, and O.

HIV Classification:

HIV belongs to the Retroviridae tribe, a part of the Lentivirus class. Two forms of retrovirus exist: (1) the oncogenic or transforming retrovirus leading to neoplasms and (2) the cytopathic or lentivirus leading to HIV. Single-stranding, positive-sense, enveloped RNA viruses spread lentiviruses. Upon entrance to the target cell, the viral RNA genome is translated by viral transcriptase (RT) that is carried with the viral genome in the virus particle into doublestranded DNA. Two forms of HIV have been characterised: HIV-1 and HIV-2, on the basis of serologic properties and sequence analysis of molecularly cloned viral genomes. HIV-1 is the originally detected virus named HTLV-III and LAV. It is more virulent, infectious and causes most HIV infections worldwide.

HIV types

The HIV-1, the main category M, the outlier group O, and two additional groupings N and P can be categorised in four categories. The most common category M is made up of nine subtypes (A-D, F-H, J and K). These Group M viruses commonly recombine and these recombinants are known as either CRF or special recombinant types (URF). In various geographic areas, diverse subtypes of HIV-1 prevail; in Africa and Eastern Europe, in America, in Europe or in Australia, subtype A, in India, China and in South Africa; in India, sub-type C. There are HIV mosaic genomes besides these subtypes. In geographic areas with more than one HIV 1 subtype circulating, these have been identified. These strains are the result of two HIV-1 sub-types which infect one single cell. The reverse

transcriptase enzyme causes the recombination to happen because of "template flipping."

Discovery of AIDS:

Around late 1980 and early 1981 AIDS was first scientifically observed. The signs of Pneumocystis carinii (PCP), an unusual opportunistic infection believed to occur in people with very disrupted immune systems, were seen by injection drug consumers and gay people with no known cause of impairment of immunity. Soon later, other gay men developed an earlier rare cancer of the skin called Kaposi's sarcoma There have been several more cases of PCP and KS that warn US Centers for Control and Prevention of Diseases quickly (CDC). To control the epidemic, a CDC task force was created. The task force identified a patient history with anomalous symptoms and named an immune deficiency syndrome acquired In contradiction to the Gallo Group study, Montagnier and his collaborators have shown that this virus has core proteins immunologically distinct from HTLV-I proteins. The party of Montagnier identified their Lymphadenopathy related virus isolated virus (LAV). The balance of the two statements was preferred for HIV. Together with his colleague Françoise Barré-Sinoussi, Montagnier was awarded one half of the 2008 Nobel Prize in Physiology or Medicine for his “discovery of human immunodeficiency virus”.

Epidemiology: Current Global Distribution of HIV:

New HIV infections have decreased according to the latest UNAID survey. HIV-1 has triggered a global pandemic in the wake of the discovery of HIV in 1983 which resulted in over 25 million deaths, and 33 million people with HIV-1 infection are estimated to have suffered from the current situation (Global distribution of HIV-1 infections seen in Figure 1.2; Statistics given by UNHO/HIV/AIDS). UNAIDS/2009 WHO's update on the global AIDS crisis reported that there were 2.6 million [2.3 million–2.8 million] newly infected individuals with HIV. It is up to a fiveth (19 percent) of those freshly infected by infection (2.9-3.4 million) in 1999, and over a quarter (21 percent) of those newly infected (3.0 million-3.5 million) in 1997, the year in which new infections reached a plateau annually. In 33 nations, the HIV incidence has dropped by more than 25 percent between 2001and 2009; 22 of these countries are in sub-Saharan Africa. It is reported that 1,8 million [1,6 million–2,0 million] persons in Subsaharan Africa, where the bulk of new HIV infections appear to occur, were infected in 2009; much smaller than approximate 2,2 million [1,9 million–2,4 million] persons in Sub-Saharan Africa, who were freshly infected by HIV in 2001. This pattern illustrates the effect of the HIV preventive work and the normal path of epidemics. This trend has a number of causes. In Western, Central, and Eastern Europe, Central Asia, and North America, the rates of annual new HIV infections have remained steady for at least the past five years. But there is growing proof of a renewal of HIV among men who have sex with men in many high income countries. In Eastern Europe and Central Asia, elevated rates of HIV transmission appear to exist in networks of people who inject narcotics and their sexual partners.

Genome organization of HIV-1:

Approximately 9200 nucleotides are in the HIV-1 Proviral RNA genome, which encompasses nine genes (gag, pol, env, tat, rev, nef, vif, vpr, vpu, and often ten tev fusion), which encrypt a total of 19 protectins.

Three important genes which contain information necessary to build new virus particle structural proteins are:

- gag: codes for the structural proteins of the nucleocapsid (group-specific antigen)
- pol: three essential enzymes codes, RT, protease (PR), RNaseH, and integraase (IN).
- env: gp160, gp120, and gp41 predecessor codes.

The remaining six genes, tat, rev, nef, vif, vpr and vpu (or vpx with respect to HIV2), have been regulatory genes for proteins that regulate HIV's cellular capacity, create new (replicate) virus copies or induce illness. Three read frames are used for transcription of HIV-1 mRNAs. After the selective splicing of primary mRNA transcripts, the HIV-1 is synthesized.

HIV-1 Life cycle:

The life cycle of HIV-1 can be divided into an early and a late replication process. The early phases begin when the virus is attached to the cellular surface and end when the proviral DNA is integrated with the hosts. The late replication of the virus lasts until it releases the virus. HIV-1 particles, mostly in the blood, lymph or lymph tissue, migrate as the inflammation is started until they bind to their target cell surface. This target cells are CD4+T-lymphocytes, which are not divided and which often produce CD4. These target cells are resting or stimulated.

Virus attachment to the host cell and entry:

HIV attachment contact between the Env gp extracells (gp120) and the CD4 antigen on prone cells surfaces accompanied by interaction with coreceptors mediates HIV attachment (members of the seven membrane-spanning CC or CXC families of chemokine receptors). CXCR4 and CCR5 are the two key coreceptors for HIV infection. As soon as the gp120 virus envelope connects to CD4 receptor and target cell coreceptor, it causes the

gp41 to change conformation and fuse the virus and cell membranes.

The membrane fusion event allows the viral centre to enter the cytoplasm of the host. HIV-1 uses CCR5 as the preferential co-receptor for transmitting the target cell but in certain situations HIV-1 used CXCR4 as the coreceptor removed from patients during the late infection period. HIV-1 isolates are also known as tropical CCR5 (R5) and tropical CXCR4 depending on the phénotype (X4 phenotype). Also recorded have been HIV-1 isolations using both coreceptors (i.e. CCR5 & CXCR4 phenotype) and ccR5 and CXCR4.

Viral uncoating and viral DNA synthesis by reverse transcription:

Uncoating of viral capsid happens inside the cytoplasm of infected cell. It is said que- sequential interaction with various cell factors and molecular rearrangements accompanying reverse transcription is supported in response to multiple consecutive shifts in cellular environments, thereby causing incremental or gradual conformational changes and disassembly.

The formation of reverse transcription (RTC) complexes and pre-integration complexes follows after uncoating (PICs). RTCs are simply classified as reverse transcription HIV-1 complexes, wherein the positive RNA viral genome is converted into double-stranded DNA. The reverse transcription of the RTC genomes is also either RNA or RNA-DNA intermediates. PICs, on the other hand, no more RNA but just dual-stranded DNA include. PICs are integration-skilled HIV-1 complexes by definition and can be integrated effectively in vitro into a goal DNA.

Integration of viral DNA into host cell chromosome:

The PIC migrate to the nucleus through microfilament and microtubules and enters the nucleus via the pathway of nuclear import. After translocation into the nucleus, the integrase cleaves the 3’ termini of the viral double-stranded DNA to produce two nucleotide 5’ overhangs at each end. The integraase then activates a transesterification reaction in which the hydroxyl 3' group destroys chromosomal DNA's phosphodiester bonds and enters viral DNA to host DNA. In certain chromosome sites, the viral DNA is spontaneously integrated. Provirus is the combined type of the virus. The not integrated linear DNA is circulated, reducing the number of linear DNA modules to the signal for apoptosis.

Transcription of viral RNA:

The virus stays dormant or is successfully transferred to the integration site and the metabolic state of the host cell according to the chromatin structure. The virus can stay latent by integrating into the areas of repressed heterochromatin, or because of lack of factors as transcriptional enhancers, such as nuclear factor Kb (NF-Kb) and Nuclear Factor of Activated T cells (NFAT). NF-KB and NFAT are linked to an enhancer LTR sequence and facilitate viral transcription in the activated cell. Host cell RNA Polymerase II attaches to the initiation site of transcription and starts transcription, but in the absence of the viral Tat protein does not elongate effectively. The tat-protein links with TAR (1) and prevents premature termination of transcription (the first viral m-RNA nucleotides is the target sequence for viral transactions).

Processing of viral RNA transcripts, nuclear export and expression of viral proteins:

Transcripts of Viral RNA are either spliced or spliced incompletely. In regulating the splicing process and transfer of viral RNA transcripts to cytoplasm, the viral Rev protein play a major role here. The cytoplasm translates these RNA molecules into viral proteins. The m-RNA molecules encoding Nef, Tat and Rev are multiplied, and the Env, Viv, Vpre and Vpu proteins are encoded in the spliced RNA transcripts. Gag (p55) and Gag-Pol (p<160) precursor proteins are encoded by unsplicated RNA transcripts. A ribosomal frame change near the 3' end of the jag is the predecessor of Gag-Pol.

Assembly, budding and maturation of HIV virus particles:

At the plasma membrane of the host cell the final phase of the viral cycle of assembling new HIV-1 virions starts. The Env polyprotein (GP160) passes through the endoplasm reticulum to Golgi, where it is cleaved through the glycoproteins gpp41 and gp120 of the two HIV envelopes. This are transferred to the host cell's plasma membrane where gp41 anchs the gp120 to the cell's membrane. At this point of the HIV development cycle, the enzyme protease plays a key role in cutting out long strands of protein into smaller sections used to construct mature viral nuclei. The Gag protein is the assembly of hIV-1 and includes all the requisite determinants for assembly so Gag itself is capable of shaping the like of viral particles, which are non-infectious. Moreover, Gag recruits other HIV-1 proteins in emerging virions, especially Env and viral RNA. Gag is synthesised as a precursor of polyprotein, Pr55gag, which is split into HIV-1 protease part subunits. The cell membrane is composed of approximately 2000 Gag proteins, 200 Gag-Pol proteins, two unplicated viral RNAs and other proteins (Vif, Vpr and Nef).These components type immature virus, which buds from the host cell using the cellular ESCRT, which mediates external vesiculation (Endosomal Sortation Complex necessary for transport). This mechanism involves the host cell, HIV-1

envelopes, including the nucleocapsid, with plasma membranes embedded with gp 120 and gp 41 proteins. Gag and Gag-Pol are intermediate proteins after the viral protease enzyme has budded. P24, 17 and other subunts form a precursor Gag Protein, while the reverse transcriptase, protease and integraase of the precursor Protein Gag-Pol is split into reverse. This leads to advanced, contagious virion development.

HIV Entry and Replication

The conformation of gp120 is modified to make an area able to associate with chemokine receptors if the HIV envelope protein Gp120 binds to CD4. The CD4-gp120 complicated association with CCR5 or CXCR4 further changes the shape of the whole envelope spike to make the gp41 touch with the host cell membrane. Gp41 inserts into the host cell membrane and facilitates the viral envelope fusion, enabling the virus to migrate effectively to the cell's innermost environment. A DC that captures the virus and sequestrates it in a specialised intracellular vacuole allows HIV to obtain entry to T cells. If the DC loaded with HIV contains a CD4+T-cell, an intercellency interface is created, called infectious synapse, which makes it possible to move the virus quickly from the DC to the T-cell. The reverse transcription of the HIV virus to establish the DNA provirus is performed after an HIV virus entered a T cell. The virus is said to be latent after it has integrated into the host cell DNA. During this preactivation period, infected T cells do not significantly transcribe the virus and only small numbers of progeny virions are generated. If either a TCR or a cytokine binding stimulates the T cell, intracellular signalling starts new transcription in the host cell. The regulatory genes of HIV begin to express themselves together with different host genes. HIV genes begin to express structural and complementary proteins as well as enzymes, accompanied by the development of progeny-virus.

HIV-1 Vpu

Structure and function: Viral U protein (Vpu) is a protein that is specific to HIV-1 and lacks HIV 2 as well as similar sives, SIV from Rhesus Macaques, plus SIV from Mangabey (SIVsmm), as a membrane-associated supplemental protein (SIVmac). In chimpanzee (SIVcpz), the HIV-1 precursor, and in Mona Monk SIVs (SIVmons), The bigger spot-nose monkey (SIVgsn), the mustache-like monkey (S IVv) and the Dent's monkey (SIVd) and the Ape, recently structural homologues were found (SIVgor). During the development cycle, two main roles are associated to the HIV-1 encoded Vpu protein. The first move is to support the down-regulation of HIV-1 CD4 receptors by protecting new CD4 molécules in the ER. The second step is Secondly, by antagonising Tetherin, which is an interferon (IFN) controlled factor in the host restriction, it improves the release of progeny virions from infected cells which directly connect virions to the host surface.

CD4 Receptor Down-regulation by Vpu:

The freshly synthesised CD4 receiver molecules in Vpu are rapidly degraded in the ER by means of the ubiquitine proteasome scheme. Once viral entry occurs, the CD4 receptor's continuous expression will harm effective viral reproduction and propagation. Previous studies have shown that freshly synthesised CD4 molécules are willing, via their strong Env binding affinity, to maintain Env precursor proteins in ER, Thereby prevents transfer and transformation to the position of the virus of the mature Env components gp120 and gp41. CD4 expression on cell surface often facilitates cell-free and cell-associated surface surface infection and can interfere with effective release from cell surfaces of infectious progeny virions. Nef destroys mature CD4 molecules early in the infection that already exist at the cell surface by increasing their endocytesis. Vpu is expressed late during viral life cycles, by comparison, and operates on CD4 molecules that are freshly synthesised in ER, which mitigate their impact on early biosynthesis.

Vpu's function in improved release of HIV-1:

Protein of HIV-1 VPU plays the second important function in promoting cell-type virus release. In the absence of Vpu, viral particles are bound to the surface of cells that contain an unauthorised virus and eventually endocytized. These tied-in virions may be released after protease, subtilisin care. It has been shown that a cellular protein known as HM1.24, CD317, BST-2 or tetherin is a subtilisin-sensitive virion inhibitor. The expression of this antigen, which can be enhanced by interferon, makes allowable cells not allowable to the loss of Vpu for HIV-1. Tetherin shall be constituted by restrictive or non-permittent cells, that require Vpu for efficient release of particles such as HeLa cells but not by HEK293T or HT1080 permissive cells. The integral membrane protein of Type II is interferon-induced, lipid raft-associated. In the absence of a vpu virion release in non-permitting cells, BST-2/tetherine rescue degradation. Vpu's position in rodent orthology in antagonising BST-2, however, is unique for species and it does not suppress BST-2 speech. At least in part VPU anticipates this protein by ubiquitin-independent pathways or retention in the transGolgi network through down-regulations from the cell surface.

Lipid rafts and HIV-1 assembly

Lipid rafts, often classified as membrane microdomains, are cholesterol-enriched plasma membrane microdomains, glycosphingolipids and other saturated lipids, and also specific protein groups. There are extremely complex bodies that may unite or separate, modulating cellular functions. According to its original description, these liquid-ordering cholesterol-dependent systems coexist with cell membrane liquids and

membrane-associated proteins, based upon their membrane binding methods, to one of these realms. Partitioning of the lipid rafts molecules in cells was determined mainly based on their relationship with DRM fractions. However, the combination of DRM only indicates preference for rafts consisting of proteins or lipids and does not indicate the precedence of the test handling of rafts. Proteins anchored in the extracellular PM leaflet using this and other methods are classified as raft-associated proteins by means of a Glycosylphosphatidylinositol (GPI) mode. Often considered to be absent from rafts are some transmembrane proteins, including transferrin receptor (TfR) and CD45.

CONCLUSION

HIV has been reported to interact with Env during virus life cycle, whether this interaction is direct or indirect is a matter of debate. Gag is considered to be the central driver of virus assembly and Gag itself can form virus-like particles. Although much is known about the function of Gag domains and their interaction with cellular and viral factors, still there are pathways and interactions that are not understood properly and needs to be delineated further. Several studies indicate that the cytometric domain Env gp41 and the Gag protein matrix are central in HIV-1 and any alterations in the region of the Gag matrix impact the integration of the envelopes in virion particles and hence the infection of the virus. Therefore, the interaction of Gag matrix with Env is crucial for appropriate HIV-1 envelope protein function. This phenomenon has also been observed in other viruses like alphavirus, Rous-sarcoma virus, Mason-Pfizer monkey virus and murine leukemia virus. Though, the data obtained from different viruses are conflicting but supports the notion that there exists a direct or indirect interaction between the Gag matrix and domains of Env. Therefore, the interaction between matrix and gp41 cytoplasmic tail seems to be vital for incorporation of envelope on HIV-1 virions.

REFERENCES

1. A.D. Frankel, J.A.T. Young (1998). HIV-1: fifteen proteins and an RNA, Annu. Rev. Biochem. 67, pp. 1–25.

2. E.O. Freed, M.A. Martin (1995). The role of the human immunodeficiency virus type 1 envelope glycoproteins in virus infection, J. Biol. Chem. 270, pp. 23883–23886.

3. R. Wyatt, J. Sodroski (1998). The HIV-1 envelope glycoproteins: fusogens, antigens, and immunogens, Science 280, pp. 1884–1888.

4. W. Weissenhorn, A. Dessen, S.C. Harrison, J.J. Skehel, D.C. Wiley (1997). Atomic structure of the ectodomain from HIV-1 gp41, Nature 387, pp. 426–430.

5. Arhel, N. (2010). Revisiting HIV-1 uncoating. Retrovirology 7, pp. 96.

6. Balliet, J.W., Kolson, D.L., Eiger, G., Kim, F.M., McGann, K.A., Srinivasan, A., Collman, R. (1994). Distinct effects in primary macrophages and lymphocytes of the human immunodeficiency virus type 1 accessory genes vpr, vpu, and nef: mutational analysis of a primary HIV-1 isolate. Virology 200, pp. 623-631.

7. Batonick, M., Favre, M., Boge, M., Spearman, P., Honing, S., Thali, M. (2005). Interaction of HIV-1 Gag with the clathrin-associated adaptor AP-2. Virology 342, pp. 190-200.

8. Ho, D.D., Neumann, A.U., Perelson, A.S., Chen, W., Leonard, J.M., Markowitz, M. (1995). Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection. Nature 373, pp. 123-126.

9. Lopez-Verges, S., Camus, G., Blot, G., Beauvoir, R., Benarous, R., Berlioz-Torrent, C. (2006). Tail-interacting protein TIP47 is a connector between Gag and Env and is required for Env incorporation into HIV-1 virions. Proceedings of the National Academy of Sciences of the United States of America 103, pp. 14947-14952.

10. Neil, S.J., Zang, T., Bieniasz, P.D. (2008). Tetherin inhibits retrovirus release and is antagonized by HIV-1 Vpu. Nature 451, pp. 425-430.

11. Schubert, U., Bour, S., Ferrer-Montiel, A.V., Montal, M., Maldarell, F., Strebel, K. (1996a). The two biological activities of human immunodeficiency virus type 1 Vpu protein involve two separable structural domains. Journal of Virology 70, pp. 809-819.

12. Varthakavi, V., Smith, R.M., Martin, K.L., Derdowski, A., Lapierre, L.A., Goldenring, J.R., Spearman, P. (2006). The pericentriolar recycling endosome plays a key role in Vpu-mediated enhancement of HIV-1 particle release. Traffic 7, pp. 298-307.

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