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HIV AND LYMPHOCYTIC NANOROBOTS

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ABSTRACT

In the present study HIV and lymphocytic Nanorobots effects are being discussed and evaluated. AIDS is a severe immunodeficiency which is a result of HIV infection. The viral RNA infects the CD4 lymphocytes, macrophages and dendritic cells and causes an intensive immunity system specific disorder. Most of the immunity system deficiencies in AIDS can be a result of CD4 cell decrease. HIV enters the cell via getting connected to both CD4 molecules and chemokine receptor family Coreceptor molecules and when inside the cell the genome will be inversely transcribed to DNA and this way it finds its way to the cellular genome. Viral gene transcription and virus production is motivated via the signals which naturally activate the host cells. Virus production happens at the price of cell death. The acute infection stage is determined by CD4 cells death present in the mucus membrane and the dispersion of the virus to the lymph nodes. In the latent stage, the virus exhibits a lesser amount of replication in the lymphomatoidal tissue and there is the slow and progressive degradation of the T-cells. The stable activation of the T-cells increases their death and leads to the fast immunity deficiency in the chronic stage. CD4 elimination in the individuals infected with HIV is a result of the viral cytopathic effect, the toxic effects of the virus products such as gp 120 and the indirect effects of the cell death as a result of CD4 activation or killing activity which is attributed to CTL. Experience has proved that if the individuals with HIV are injected with immunity-suppressing drugs (the immunity system weakening drugs which are used for preventing from the binding) the same way that the individual's immunity system is disrupted the HIV virus is also deactivated and it will no longer

be able to transform nor it will be capable of infecting the healthy cells and under such circumstances the HIV genome can be identified in the body of the individual with HIV and by the injection of the nanorobots identified for genome-bearing cells phagocytose the HIV virus and the infected cells can be extracted from the individual's body and the individual's body can be cleared from the viral traces.

Keywords: HIV, lymphocytic nanorobots, cell death, CTL

INTRODUCTION

During the past two decades, AIDS has been the major cause for the death of over 11 million people around the world. And there are more than 33 million people diagnosed to have AIDS for the time being which is going to double within several years from now. HIV destroys the human immunity system and leaves the body defenseless against most of the diseases. Even though there has been a lot effort globally to control and treat HIV, AIDS is still cureless. During the past several years, a novel medicinal complex has effectively controlled AIDS progress and has tangibly reduced the morbidity caused by HIV in the US and other developed countries. These therapeutical medicines fight the virus in various ways. Therefore, in the current situation the conditions are in favor of the drug resistant virus which is a general challenge caused by single medicine therapy and, on the other hand, multidrug therapy regime is a difficult and tedious process for the patients and the expensive nature of the drugs makes their use limited even for the rich individuals. Besides, some of the patients cannot bear the drugs side effects. While some of the medical researchers are active in the field of drug improvements they have not gained favorable results yet. Therefore, at present the only weapon we have against HIV is instruction and training. World Health Organization (WHO) has agreed with the Magic Johnson method which is based on riskless sexual relationships (decreasing the number of the sex partners and using condoms) and it is also dealing with offering advertisements regarding this subject. These instructions and advertisements have been effective and useful up to the recent decade and have brought about considerable reductions in the number of the people with AIDS.

The importance and the necessity of the subject matter:

1. Nowadays, with the existing economical conditions, people's poor monetary conditions, the reduction of the tendencies to marriage in youths

and the condoms being changed into a luxurious and expensive commodity and thousands of other reasons has led to neglecting the "Magic Johnson" method and increasing in the illegitimate and of course highly risky sexual relationships in the developing countries. So, it is clear that producing an effective HIV vaccine is of the utmost priority. Various types of vaccine manufactured by using various traditional and novel methods have been experimented with the animals and humans. But, due to the fast and perpetual transformation and mutation of HIV none have an acceptable result. Therefore, we have tried to present the reader with a comprehensive article regarding the HIV process in the body and offer an unprecedented therapeutical method through blending the biological and NANO sciences which has not ever been tested in the world level and it is hoped that by the grace of the God almighty we become the first who offers an absolute treatment for AIDS.

THE OBJECTIVES:

2. **The nanorobotic lymphocytes production aiming at the AIDS absolute treatment and using it for the other ailments**
3. **Definitions and expressions:**

CNS: central nervous system;

Lentivirus: viruses with slow replication feature;

Retrovirus: viruses with inverse transcriber enzymes;

Cytopathic: viruses causing cells structural changes in the cell culture

Antigenicity: a viral protein capability for inducing the immunity system

Clinical syndrome: a group of the clinical demonstrations expressed in a given disease;

LTR: the ending recurrent sequences;

KD: (kilo Dalton) molecular measurement unit;

120gp: 120-kiloDalton glycoprotein which is the most important HIV virus receptor;

41gp: 41-kiloDalton glycoprotein causing the virus membrane and cell membrane merge;

160gp: 120gp and 41gp primer;

Integrase: viral enzyme causing the integration of the virus genome with the host cell genome;

Env: one of the most important gp producers;

CD4: the ancillary T lymphocytes marker;

Receptor: receiver;

Chemokine receptor: immunity system mediators' receiver;
Proteolytic: enzymes with protein breaking characteristics;
Coreceptor: ancillary and assisting receptor;
Virion: perfect and pathogenic virus;
Mutation: gene alteration;
CTL: killer T-lymphocytes;
Crystallography: a technique for determining the virus structures;
Cofactor: ancillary factor;
P: protein;
Uracil mutations: RNA organic bases;
Epithelium: a type of cutaneous cells;
Macaques: a type of monkey;
Doman Lectin: an area of the receptors;
Mannose: blood sugar;
Viremia: the existence of virus in the blood;
Apoptosis: cell controlled death (cell suicide);
Toxic: poisonous;
Process: procedure.

THE STUDY METHODOLOGY AND FINDINGS:

HIV is a member of the Lentiviruses family from the animal retroviruses. Lentiviruses include the sheep and cattle Visna virus, and it is the monkeys' immunodeficiency virus (SIV) which is capable of creating long latent infection in the cells and short-range cytopathic effects which gradually leads to a progressive and fatal disease which comprises the degradation syndromes and CNS destruction. Two of the related HIVs are HIV1 and HIV2. HIV1 is the most common cause for AIDS, although HIV1, 2 differ in their genome and antigenicitic structures they both create similar clinical syndrome.

A HIV infectious particle includes two similar RNA chains which are placed inside the viral proteins nucleus and are covered by two phospholipid layers derived from the host cells membrane but they also include the membrane proteins codified by the virus. HIV RNA genome is almost 9.2 kilobase (Kbp) long and its main nucleic acid sequences order is characteristic of all of the known retroviruses. The recurrent long ending areas (LTR) in each of the genome's ending parts adjust the virus merge into the host genome, gene expression and viral replication. gag sequences encode the nucleus structure proteins. env sequence encodes the 12gp and 41gp membrane glycoproteins which are required for the cell infection. pol sequences of the inverse transcribing enzyme encode the integrase and protease enzymes required for the virus replication. Besides these known genes, HIV1 virus is comprised of six adjusting genes named tat, rev, vif, nef, vpr, and vpu

the products of which adjusts the virus production in various paths.

Cells' HIV infection instantiates when the covering glycoprotein (Env) of a viral particle binds to CD4 and the ancillary receptor which is a member of the chemokine receptors family. The virus particles which are the cause of the infection instantiation are present in the individual's blood, semen liquid or the other body liquids and they are transferred to the other individual via sexual intercourse, syringe or via the placenta. Env complex is comprised of a subunit of intramembranous 41gp and a 120gp external subunit which are connected to each other via a covalent bind. These subunits are created via the 160gp proteolytic cleavage.

Env complex is expressed as a triple structure made up of three pairs of 120go-41gp. This complex causes the multistage virion coverage with the target cell membrane. The first of this process is the 120gp subunit connection to the CD4 molecule which causes a spatial change and the next 120gp connection to the coreceptor (ancillary receptor) strengthens the chemokine. The coreceptor connection causes a spatial change in 41gp which exposes a hydrophobic region which is called connective peptide and it enters the cell membrane and enables the virus membrane to connect to the target cell membrane. After the completion of the virus life cycle in the infected cell, the free viral particles are released from the infected cell and they connect to another uninfected cell, therefore the infection dispersion takes place. Moreover, 120gp and 41gp which are expressed on the infected cells plasmic membrane can cause a cell-to-cell connection with a coreceptor expressive cell and an uninfected CD4 and HIV genome can be directly passed through the connected cells. The CD4 and chemokine receptors identification as the HIV receptor has been confirmed via different experimental examinations and clinical observations. CD4 was firstly proposed as the virus receptor and this was due to this fact that only the selected CD4 cells were destroyed in the individuals with HIV and in invitro experiments they were the CD4 cells which were infected by HIV. The studies regarding the connection to the receptor by using the purified recombinant molecules have justified that 120gp makes a specific connection to CD4 and the mutation and X-ray crystallography has determined the regions these two molecules react physically with one another. The need for a coreceptor other than CD4 has been doubted in HIV studies, firstly, because the human recombinant CD4 expression did not make the cell prone to the HIV infection

in many of the nonhuman cell lines, but the infection took place in the consequent human cells connections. The preliminary justification of a chemokine receptor acting as cofactor for HIV entering the cell was conducted through the human cDNA library screening for surveying the human CD4 expressive mouse cell line which can be infected by a HIV positive mouse inclined towards the T-cell line. cDNA separated which encodes the chemokine receptor CXCR4 connects to SDF-1a and SDF-1b.

The most important chemokine receptors which act as the HIV coreceptor are CXR4 and CCR5. More than seven types of chemokine receptors have been demonstrated which act as the coreceptor for HIV entrance to the cells and several other proteins belonging to the receptor family associated to G protein which moves seven times across the membrane such as Leukotriene B4 receptor are regarded as the HIV infection intermediator. Various isolates are with different tendencies for various cell populations which is related to the 120go varieties characteristics for the various chemokine receptors. All of the HIV stubs can be infectious and replicate in the human CD4 cells separated recently and they can be activated invitro. In contrast, some of the stubs (early culture from the human macrophages and not in the continuous T-cell lines) infect the M-inclined virus or macrophage-inclined virus, while other stubs (T-cell lines and not in the macrophages) infect the T-inclined virus. Some of the viral stubs infect both the T-cell lines and the macrophages. Macrophage-o-phil virus isolates express a 120gp which is connected to CCR5 and it is expressed on some of the macrophages and some endangered T-cells, while the T-cells inclined viruses connect to CXCR4 which are expressed on T-cells. HIV X4 variants has the ability to connect to both of the chemokine receptors for binding with CXCR4 and R5 for connecting to CCR5 and X4R5. In many of the HIV infected individuals one variant of the virus production uses the CCR5 and it is inclined towards the macrophages during early stages of the disease and it binds with CXCR4 and it is inclined toward the T-cell line in the later stages. T-tropic stubs are pathogenic. Probably, due to this reason that they eliminate more of the infected cells respective to the M-tropic stubs. The importance of the CCR5 in HIV infection and invivo is supported by this finding that the individuals who do not express this receptor are infection resistant as a result of genetic mutations.

When a HIV virion enters a cell, the enzymes are activated inside the nucleoprotein complex and the virus replication cycle begins. The mature infectious viral particles synthesis is instantiated after the perfect viral RNA copies are produced and the virus genes are expressed in the form of protein.

The intact T-cells are resistant to the HIV infection since these cells possess an active form of an enzyme which enters the mutation in the HIV genome. AIDS sickness starts with an infection which is partly controlled to some extent by a specific immunity response and then it shifts to the progressive and chronic form which triggers the peripheral lymphocytic tissues. Transferring from the acute phase to a chronic phase of the disease can be determined via the virus propagation, viremia and the host immunity response. After the acute preliminary infection phase the chronic phase is followed during which the lymphocytic nodes and spleen are the hot spots for the HIV continuous replication and cell destruction. The main reason behind CD4 cells deficiency in the patients with HIV is due to the infection direct cytopathic effects of HIV infected cells.

DISCUSSION AND CONCLUSION

There has not been found any cure for AIDS since this virus transforms very fast and it is possible for it to be present in one individual's body with several different genomes. So, it is clear that for producing an effective and efficient accompanied with a successful treatment method we should do something to lock the HIV virus and prevent it from transformation. At present, patients with AIDS consume drugs which strengthen their immunity system but experience has proved that if the AIDS-infected individual's body immunity system can be weakened by the use of the immunity-killing drugs (drugs which are used for the patients receiving an organ in order for the connection not to be rejected) or it can be ceased from performing, the HIV virus can be locked and it also stops from working that is to say that it cannot transform or infect another cell. But, as you know HIV, itself, weakens the immunity system and if we intensify this action by using the immunity killing medicines the individual's body is left defenseless and it is possible that s/he dies after a few hours. So, in order to be able to use immunity killing drugs we have to find a substitution for the body's immunity system which cannot be disrupted via using the immunity killing medicines and quite contrary it can be HIV resistant. Our suggestion is the use of Nanorobots. Robots produced in Nano scales and they can enter our bodies and play on behalf of the

lymphocytes. This robot can be made with an information bank containing the characteristics of all of the pathogenic factors and the friendly cells. This intelligent robot circulates in the bloodstream in the entire body and in case of observing a suspicious factor it can scan the factor and search its characteristics in its information bank and if it is a threatening pathogen it will be destroyed.

And from one hand, another group of these Nanorobots containing the HIV genome features existing in the patient's body can be entered into the body in order to phagocytose the cells and viruses possessing the existing genomes in the information bank and excrete them from the body. After we are assured that there exists no trace of the HIV in the body, it can be gradually recover itself via the basic cells or the immunity boosting drugs and then the Nanorobots can be extracted from the body. Of course, such Nanorobots can be wonderfully effective on the overwhelmingly large number of diseases.

We hope that this robot which has not been studied in any place in the world and its production can be a huge revolution in the medical sciences can be produced from the first time in Iran and from there to the world.

And in the end, it can be said that many of the diseases including the chronic AIDS disease can be cured through lymphocytic nanorobots production.

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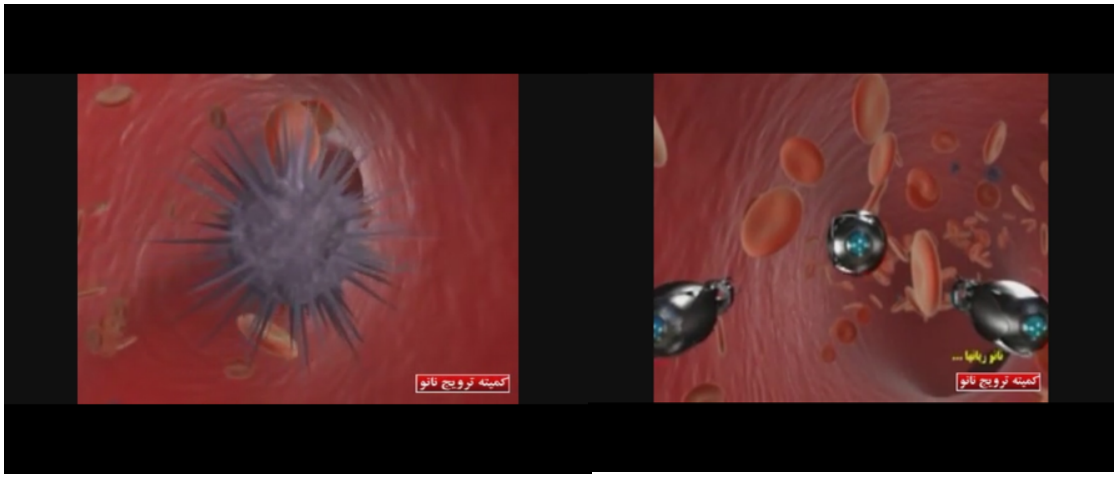
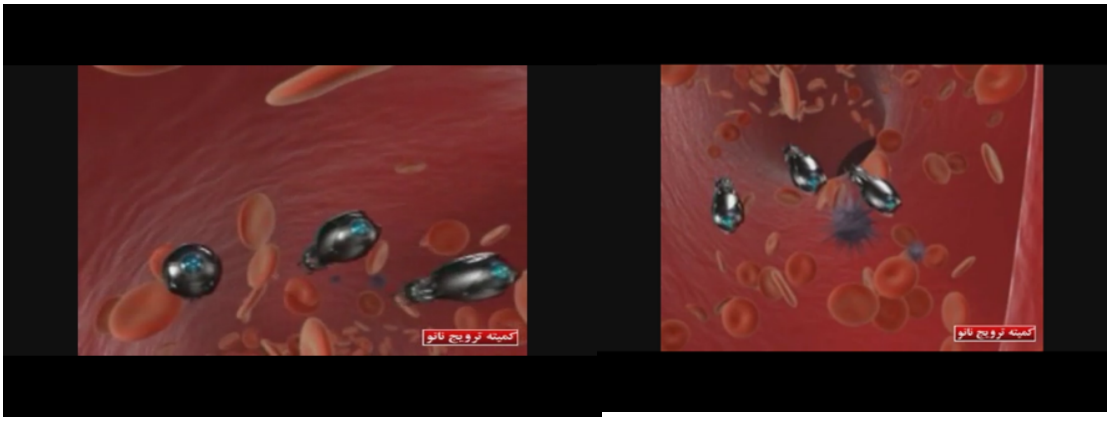
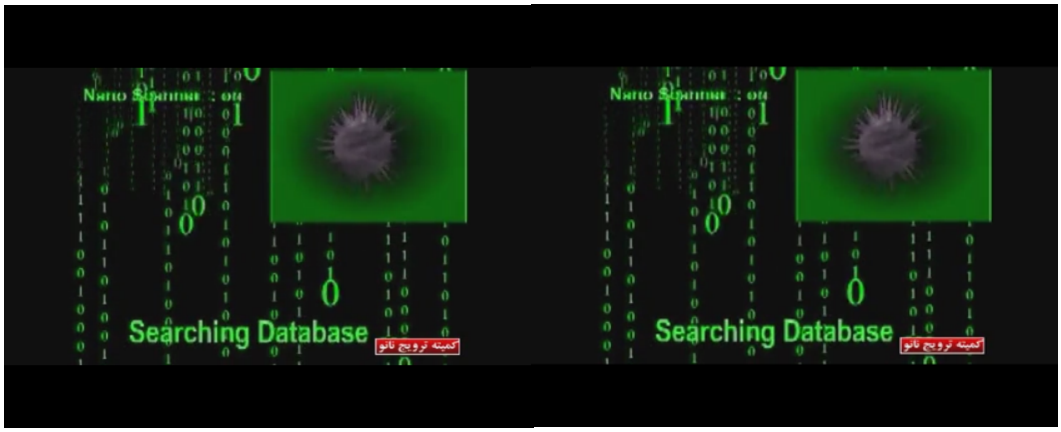
4. Attachment:

Nano promotion committee



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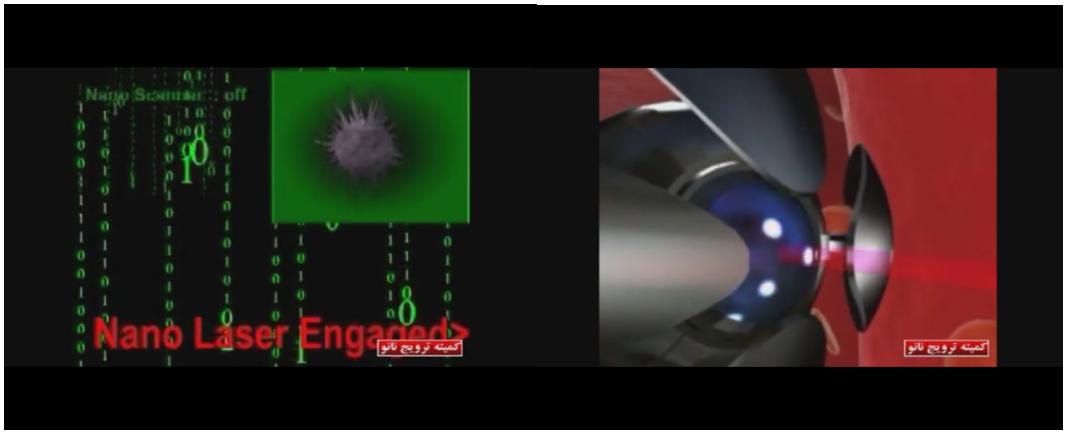
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