Winning The Battle Against HIV-1

I Secasan, D Pop, C Secasan

Citation

I Secasan, D Pop, C Secasan. *Winning The Battle Against HIV-1*. The Internet Journal of Infectious Diseases. 2006 Volume 6 Number 1.

Abstract

Objective: To present an entirely new theory and practical solution to completely eliminate HIV-1 from the human body, based on a combination between a HAART regimen (HAART-x) and a corresponding, pre-administrated-to-(HAART-x), therapeutic vaccine (Vaccine-x) made of short HIV-1 DNA-sequences containing the point-mutations (resistance-mutations-pattern) that would be induced into HIV-1's genome by the corresponding, following, to come, HAART regimen (HAART-x).

Design and methods: HIV-1's ability and need to mutate under HAART pressure is exploited, and the synergetical scissoring effect on HIV-1 of each
(Vaccine, HAART)-couple is used to eradicate HIV-1 from the human body. Knowing in advance, the HIV-1 resistance - mutations - pattern for each antiretroviral drug, and also for any HAART or Mega-HAART regimen, (e.g. from Stanford University HIV Drug Resistance Database, http://hivdb.stanford.edu/), HIV-1 DNA therapeutic vaccines can be designed, produced and administrated to HIV-1 positive patients, prior to their usual, corresponding HAART regimens, and these HIV-1 DNA therapeutic vaccines prevent and hinder the emergence of drug-resistant HIV-1 (or HAART-resistant HIV-1), and thus contribute together with HAART, to the eradication of HIV-1 from the human body, and cure AIDS.

Results:The general HIV-1 eradication scheme is a succession, or series, of (Vaccine-x, HAART-x)-couples:
(Vaccine-1, HAART-1) ---> (Vaccine-2 , HAART-2) ---> (Vaccine-3 , HAART-3) --->.....---> (Vaccine-x , HAART-x) --->.....---> (Vaccine-n , HAART-n)---> Eradication
and indicates that each therapeutic-vaccine (Vaccine-x) is pre-administrated to its corresponding (HAART-x) regimen.
Also, each anti HIV-1 therapeutic-vaccine (Vaccine-x) is made of short HIV-1 - DNA - sequences which contain the point-mutations (resistance-mutations-pattern) that would be induced into HIV-1's genome by the corresponding, following, to come, HAART regimen (HAART-x).

Conclusions:
HIV-1 can be be eliminated from the human body, by treatment with successive (Vaccine-x, HAART-x)-couples, followed by (Vaccine-x , Mega-HAART-x)-couples

INTRODUCTION

Time has come for Science and Medicine to win the battle against HIV and AIDS. Since a classical vaccine against HIV-1 is hard to design or even define, and since current HAART (highly-active-anti-retroviral-therapy) and even Mega-HAART regimens are unable to clear an HIV-1 infection, a combined strategy has to be adopted, in order to achieve HIV-1 eradication.

This article presents an entirely new theory and practical solution to eradicate HIV-1 (from the body of HIV-1 infected persons), based on HIV-1's ability and need to mutate under HAART (or Mega-HAART) pressure, and on the synergetical scissoring effect on HIV-1 of successive (Vaccine-x,HAART-x)-couples, which are each formed of:

1. a therapeutic-vaccine (Vaccine-x) consisting of short DNA-sequences of HIV-1 which contain (or bear in their biochemical structure) the point-mutations (PM),

(resistance-mutations-pattern , RMP-x) that would be

induced into HIV-1's genomic blueprint (biochemical structure) by the following, to come, HAART-x regimen;

and of

2. the corresponding, following, (HAART-x) regimen itself.

DESIGN AND METHODS

HIV-1 recombination and mutation ([1,2,3,4,5,6]), including "resistance-mutation", are important mechanisms by which HIV-1 evades drug or immune pressures.

HIV-1- strains that are resistant to an antiretroviral drug present multiple " point-mutations" (PM), which act in synergy to confer the resistant phenotype to that drug, and we may define these "point-mutations" as resistance-mutations-loci (RML) or resistance-mutations-sites (RMS), whereas their ensemble may be termed as resistance-mutations-pattern (RMP).

Multidrug resistant HIV-1 strains arise in patients treated with HAART or Mega-HAART regimens, either through direct mutation or through recombination of variants that are resistant to single drugs.

Paradoxically, and luckily at the same time, point-mutations (PM) that confer drug - resistance, and consequently the whole resistance-mutations-pattern (RMP-x) of a (HAART-x) regimen offers us the complete biochemical information, for the development of very specific and powerfull vaccine(s) and therapeutic vaccines (Vaccine-x) against HIV-1.

The drug-induced point-mutations (PM) on HIV-1's genome, i.e. the resistance-mutations-loci (RML) or resistance-mutations-sites (RMS), and even the whole resistance-mutations-pattern (RMP) of any particular (HAART-x) regimen may be introduced, (in form of short HIV-1-DNA-sequences which contain the point-mutations) in a multivalent, polivalent or multivalent-polivalent-therapeutic-vaccine (Vaccine-x) aimed to prevent the emergence of (HAART-x) - resistant HIV-1 virus.

If (Vaccine-x) is now preadministrated to (HAART-x), the emergence of (HAART-x) - resistant HIV-1 virus is prevented, and thus (HAART-x) will eradicate HIV-1 from the blood and body of infected individuals.

In HIV-1 infection, the infected hosts apparently cannot solve the problem of identifying an antigen that is conserved among the variants and quasispecies, and thereby neutralize the infection. Paradoxically and luckily again, both HAART and/or Mega-HAART regimens are not only reducing HIV-1 viral loads to 50 copies/ml or less, but they are also "UNIFYING" HIV-1's genetic diversity, by "artificially" creating a "common factor" among the remaining/surviving (50-400) copies/ml of HAART-resistant-HIV-1, in form of these point-mutations (PM), (i.e. resistance-mutations-loci, resistance-mutations-sites), which together build the resistance-mutations-pattern (RMP).

The list below presents the point-mutations induced by a particular antiretroviral drug, (or by a combination of antiretroviral drugs), into HIV-1's genomic blueprint.

Drug / Primary Resistance Mutations / Mutations With Additional Effect
AZT (Retrovir®) / M41L, T215Y, T215H / D67N, K70R, K219Q, K219E
3TC (Epivir®) / M184V, M184T, M184I / -
ddI (Videx®) / L74V / K65R, L74V, V75T, M184V
ddC (HIVID) / K65R / T69D, L74V, V75T, MI84V, Y215C
Abacavir (Ziagen) / - / K65R, L74V, Y115F, M184V
D4T (Zerit®) / V75T / 150T
Nevirapine (Viramune®) / K103N, Y181C, Y181I / A98G, L100I, V106A, V108I, Y188C, G190A
Delavirdine (Rescriptor®) / K103N, K103T, Y181C / P23L
Efavirenz (Sustiva) / Y188L / L100I, K101E, K103N, V108I, V179D, Y181C
Indinavir (Crixivan®) / M46I, M46L, V82A, I84V / L10I, L10R, K20M, K20R, L24I, V32I, I54V, A71V, A71T, L90M
Nelfinavir (Viracept®) / D30N, M46I, A71V, I84V / M36I, V77I, N88D, L90M
Saquinavir (Fortavase®) / G48V, L90M / L10I, I54V, I84V
Ritonavir (Norvir®) / V82A, V82F, V82S, I84V / K20R, L33F, M46I, I54L, I54V, A71T, A71V, L90M
Resistance to multiple drugs
AZT + ddI/ddC / A62V, V75I, F77L, F116Y / Q151M (all 4 mutations are required for significant resistance)
AZT + 3TC / M184V + R211K + L214F / G333D, G333E

A very large database containing nearly all published HIV-1 reverse-transcriptase and protease sequences, and that allows for mutations searching can be found at :

http://hivdb.stanford.edu/ , namely the Stanford University HIV Drug Resistance Database . Likewise, The Los Alamos HIV Drug Resistance Database(http://resdb.lanl.gov/Resist_DB/default.htm) is a compilation of mutations in HIV genes that confer resistance to anti-HIV drugs. Both databases can now be used not only

for the design of new antiretroviral drugs and anti-HIV-1 vaccines, but also for the design and creation of therapeutic vaccines against HIV-1 (Vaccine-x), to be used in (Vaccine-x , HAART-x) - couples.

An excellent review about HIV-1 therapeutic vaccines ([7]) and an article about the role of therapeutic vaccines in the control of HIV-1 in the HAART era ([8]) have been published by Kinloch-de Loes and Autran ([7, 8]).

With the availability of HAART, an unique opportunity arises and exists, to enhance anti-HIV immunity by adding anti-HIV-1 therapeutic vaccines as an additional therapeutic option for HIV-infected patients, which will proove to be critical to the conversion of HIV/AIDS to a manageable long-term infection, and ultimately to HIV/AIDS eradication. HAART offers new opportunities for the design of new therapeutic immunisation strategies. An anti-HIV-1 therapeutic vaccine is meant to treat existing HIV-1 infections. More of a treatment than a vaccine in the classic sense of the word, a therapeutic vaccine against HIV-1 is meant to teach the immune system to fight the existing infection. In theory, a therapeutic vaccine should reduce the severity of an infection that already exists, and in a best-case-scenario, it should direct the immune system to the point where the infection is completely controlled and finally eliminated.

Using an “ad conventium” terminology, a multivalent therapeutic vaccine (MTV-x) against HIV-1, should be designed to elicit an immune response to several different antigenic determinants of a single pathogenic agent or a single strain (e.g. a single strain of HIV-1). In multivalent vaccines, the optimal association or combination of antigens must be assessed to obtain synergistic effects. For example, a multivalent therapeutic vaccine made of short HIV-1 sequences which contain the resistance-mutations A62V, V75I, F77L, F116Y and Q151M should be pre-administrated to the triple drug combination AZT + ddI/ddC in order to achieve the best results in terms of viral reduction.When the drug combination (AZT + 3TC) is used as the drug component of the (Vaccine-x , HAART-x)-couple, it should be preceded by a multivalent therapeutic vaccine (Vaccine-x) made of short HIV-1 sequences which contain the resistance-mutations M184V + R211K + L214F / G333D, G333E in order to achieve a powerful synergetical effect in HIV-1 viral reduction. As can be seen, we have chosen the drug-resistance-point-mutations of HIV-1 as antigenic determinants, to be used in therapeutic vaccines against HIV-1, and these therapeutic vaccines against HIV-1 (Vaccine-x), prevent the emergence of HAART-x resistant HIV-1, when pre-administrated to (HAART-x) - which eliminates the HAART-x sensitive HIV-1. In this way (Vaccine-x , HAART-x) - couples can efficiently fight HIV-1 and eliminate it.

Each drug-induced-point-mutation, or each HAART-x - induced-point-mutation (PM), taken separately, can be used as a simple therapeutic-vaccine (STV-x) against HIV-1. Simple therapeutic vaccines (STV-x) against HIV-1, may also be used in couples with both single antiretroviral drugs, or with multiple drugs, or with HAART-x regimens. For example, a simple therapeutic vaccine (STV-x) based on point-mutation M41L can be used together with AZT (Retrovir®) monotherapy in a simple couple termed as (Vaccine-M41L, AZT (Retrovir®)). Another simple therapeutic vaccine (STV-x) based only on point-mutation A62V can be used e.g. together with 3 drugs (AZT + ddI/ddC) in a couple termed as (Vaccine-A62V , AZT + ddI/ddC). Of course, a multivalent therapeutic vaccine (MTV-x) based on an entire resistance-mutations-pattern (RMP) like (Vaccine -A62V, V75I, F77L, F116Y, Q151M) and used in a couple termed as (Vaccine -A62V, V75I, F77L, F116Y, Q151M , AZT + ddI/ddC) would be probably more efficient against HIV-1 than the couple (Vaccine-A62V , AZT + ddI/ddC), which is based on a simple therapeutic vaccine only, namely Vaccine-A62V.

A polyvalent therapeutic vaccine (PTV-x) against HIV-1 would be one prepared from antigens, of at least two different strains of HIV-1 and it should be able to efficiently prevent the emergence of at least two different HIV-1 strains. The antigens of such a polyvalent therapeutic vaccine (PTV-x) against HIV-1 would consist of short DNA-sequences which include the point-mutations of at least two different HIV-1 strains. A polyvalent therapeutic vaccine (PTV-x) should have the capacity to prevent the emergence of at least 2 resistance-mutations-patterns which would be generated by at least 2 different, successive HAART-x (or Mega-HAART -x) regimens, or it should be able to prevent the emergence of at least two successive resistance-mutations-patterns which would be generated by the use of a HAART-x regimen.

A multivalent-polyvalent therapeutic vaccine (MPTV -x) against HIV-1 should be able to prevent the emergence of a very high number of successive resistance-mutations-patterns (RMP-s) which would be generated by a single HAART-x (or Mega-HAART -x) regimen and, ideally, it

should be able to eradicate HIV-1 by acting synergetically with all possible successions of HAART-x or Mega-HAART-x regimens, and/or by preventing the emergence of all HIV-1 resistance-mutations-patterns that would be generated by successive HAART-x or Mega-HAART-x regimens, till eradication.

Interestingly and noteworthy, within each (Vaccine-x , HAART-x)-couple, and by analogy within each (Vaccine-x , Mega-HAART-x)-couple, the (simple, polyvalent, multivalent, or multivalent-polyvalent) therapeutic vaccine (Vaccine-x) acts in fact like a true vaccine, like a CLASSICAL VACCINE, against the HAART-x-resistant HIV-1 virus (or Mega-HAART-x- resistant HIV-1 virus), by preventing its emergence.

Each antiretroviral drug, and any HAART-x or Mega-HAART-x regimen, divides the HIV-1 viral population in two:

1. drug-sensitive-HIV-1, - which is eliminated by the respective antiretroviral drug , HAART-x , or Mega-HAART-x regimen

2. drug-resistant-HIV-1, - whose emergence can be prevented when the therapeutic vaccine (Vaccine-x) , (made of short HIV-1 sequences which bear/contain the point-mutations that would be generated by HAART-x or Mega-HAART-x on HIV-1's genome), is pre-administrated to HAART-x (or Mega-HAART-x) respectively.

If a pre - HAART-x administrated therapeutic vaccine (Vaccine-x) manages to prevent the emergence of HAART-x-resistant-HIV-1, then an HIV-1 infection can be cleared and eradicated from the body of an HIV-1 infected patient, since the corresponding , following, to come HAART-x-regimen will eliminate the HAART-x-sensitive-HIV-1.

RESULTS

The general HIV-1 eradication scheme is a succession, or series, of (Vaccine-x, HAART-x)-couples:

(Vaccine-1, HAART-1) ---> (Vaccine-2 , HAART-2) ---> (Vaccine-3 , HAART-3) --->.....---> (Vaccine-x , HAART-x) --->.....---> (Vaccine-n , HAART-n)---> Eradication and indicates that each therapeutic-vaccine (Vaccine-x) is pre-administrated to its corresponding (HAART-x) regimen.

(x is an integer, which takes values from 1 to n)

By “corresponding (HAART-x)” regimen we understand the HAART-regimen which would induce into HIV-1s genome a resistance-mutations-pattern (RMP-x) which is prevented from emergence by the pre-administration of the therapeutic vaccine (Vaccine-x).

Of course, if the eradication of HIV-1 from the body of HIV-1-infected patients cannot be achieved by a succesion of (Vaccine-x, HAART-x)-couples, a succesion or series of (Vaccine-x , MegaHAART-x)-couples should be employed in order to eliminate HIV-1.

Two Latin sayings explain the rationale of using (Vaccine-x , HAART-x)-couples or (Vaccine-x , Mega-HAART-x)-couples in the eradication of HIV-1.

“Divide et Impera” perfectly describes the role and action of HAART-x regimens (or Mega-HAART-x regimens), which divide the HIV-1 viral population in HAART-x-sensitive-virus (which is eliminated/cleared by HAART-x) , and HAART-x resistant-virus , whose emergence is prevented by the therapeutic vaccine (Vaccine-x).

Therapeutic vaccine (Vaccine-x) is always pre-administrated to HAART-x according to the main principle of prevention, vaccination and homeopathy “Similia Similibus Curentur” , and in fact, this therapeutic vaccine against HIV-1 (Vaccine-x) acts like a classical vaccine within its corresponding (Vaccine-x , HAART-x)-couple.

Infection and immunity are two sides of the same coin.

Therefore it is reasonable and scientifically sound to vaccinate an HIV-1 positive person with a therapeutic-vaccine (Vaccine-x) consisting of short DNA-sequences of HIV-1 which contain or bear the individual point-mutations (PM-x), (which together represent the entire resistance-mutations-pattern , RMP-x), which would be induced into HIV-1's genomic blueprint (biochemical structure) by the following, to come, HAART-x regimen.

At the end of the HIV-1 eradication process

(Vaccine-1, HAART-1) ---> (Vaccine-2 , HAART-2) ---> (Vaccine-3 , HAART-3) --->.....---> (Vaccine-x , HAART-x) --->.....---> (Vaccine-n , HAART-n)---> Eradication a last therapeutic-vaccine (Vaccine - n+1) should be administrated, (during therapy with HAART-n), consisting of the same short DNA-sequences, but of unmutated, wild-type HIV-1, since it is well known that HAART-x (or Mega-HAART-x)-mutated HIV-1 virus tends to revert back to wild-type HIV-1 when antiretrovital

treatment is stopped or temporarily interrupted (structured-treatment-interruption -STI). This vaccination with short DNA-sequences of wild-type HIV-1 virus should be done shortly before HAART-n or Mega-HAART-n therapy is stopped (or before previously planned structured-treatment-interruptions), since it is well known that some wild-type HIV-1 may still be hidden in certain organs or tissue reservoirs and since it is also well-known that eventually surviving HAART-resistant- HIV-1 virus tends to revert to wild-type HIV-1 virus, after HAART-treatment is stopped.

The process of HIV-1 eradication may be divided in 3 main steps, by monitoring HIV-1 viral load decreases:

STEP 1 would mean a viral load decrease from 60.000 copies/ml or higher, to 50-400 copies/ml;

Current HAART and/or Mega-HAART- regimens make STEP1 possible for some years, but are unable to eliminate .an existing HIV-1 infection and thus they are unable to cure AIDS. Even more, HAART and/or Mega-HAART- regimens (even when combined with any presently available therapeutic vaccine (like e.g. Remune), or with any presently available anti HIV-1 classical vaccine - used as a therapeutic vaccine), are unable to keep viral loads low or undetectable for decades or for a lifetime, which would transform an HIV-1 infection into a long-term or lifelong manageable disease.

Our combination of a single (HAART-x) regimen and of its corresponding (multivalent or polivalent) therapeutic vaccine (Vaccine-x) pre-administrated to (HAART-x), which we have termed as a (Vaccine-x , HAART-x)-couple in this article, would probably achieve superior results to any HAART or Mega-HAART regimen combined with any presently available therapeutic vaccines, because the components of the (Vaccine-x , HAART-x)-couple act in an optimal synergy. In conclusion, a single (Vaccine-x , HAART-x)-couple would make STEP1 possible, STEP 2 would mean a viral load decrease by further 3 orders of magnitude, from 50-400 copies/ml to 50-400 copies/litre, by employing two or more successive(Vaccine-x , HAART-x)-couples.

STEP 3 would mean a further viral load decrease from 50-400 copies/litre to zero copies/litre, i.e. eradication of HIV-1, by employing successive series (and even cycles of successive series of (Vaccine-x , HAART-x)-couples in repeated cycles, eventually followed by successive (Vaccine-x , MegaHAART-x)-couples, eventually also in repeated cycles. In order to achieve complete eradication of HIV-1 the complexity of the (Vaccine-x) component of the successive (Vaccine-x , HAART-x)-couples should be gradually increased from a simple therapeutic vaccine (STV-x) to a multivalent therapeutic vaccine (MTV-x) and from here to a polyvalent therapeutic vaccine (PTV-x) and finally to a multivalent-polyvalent therapeutic vaccine (MPTV -x).

In order to better illustrate the potential anti-HIV-1 power of a couple formed by a multivalent therapeutic vaccine (MTV-x) and its corresponding HAART-x - regimen, it can be estimated that such a couple (MTV-x, HAART-x) would be 1000 times (3 orders of magnitude) more efective in reducing viral load than the respective HAART-x - regimen alone, and this estimate is based on the synergy, complementarity, optimization and perfect coordination between the two components of the (Vaccine-x, HAART-x)-couple. A single antiretroviral drug like AZT (Retrovir®) , would become as effective as 3-4 antiretroviral drugs (i.e. as effective as a HAART-regimen) in reducing HIV-1 viral load, provided that it is preceded by a multivalent-therapeutic-vaccine (MTV-x) consisting of short DNA-sequences of HIV-1 which contain (or bear in their biochemical structure) the point-mutations (PM) which would be induced into HIV-1's genomic blueprint (biochemical structure) by AZT (Retrovir®) , namely M41L, T215Y, T215H / D67N, K70R, K219Q, K219E. We may write the (Vaccine-x , Drug-x) - couple for AZT (Retrovir®) as (Vaccine-M41L, T215Y, T215H / D67N, K70R, K219Q, K219E , AZT-Retrovir®).

Affymetrix (http://www.affymetrix.com/index.affx), a world-leading US company in DNA-chip technology, has developed GeneChip oligonucleotide probe arrays that are manufactured using a high resolution photolitographic fabrication process adapted from the semiconductor industry, for HIV-1 mutations determinations. (A database of companies which are active in the biochips industry can also be found at http://www.biochipnet.com/companies). Affymetrix GeneChip oligonucleotide probe arrays can be used for the very precise identification and determination of drug-induced HIV-1 mutations, and for the development of vaccines and therapeutic vaccines (Vaccine-x) against HIV-1, to be used in (Vaccine-x , HAART-x) - couples.

At this point the legitimate question arises about how short the DNA-sequences of HIV-1, (which contain/bear in their biochemical structure the point-mutations (PM), that would be induced into HIV-1's genomic blueprint by the following, to come, HAART-x regimen), should be or can be, so that

we can see an optimal immune response against the emergence of HAART-x resistant HIV-1 ? We believe that the shortest DNA-sequences of HIV-1, (which contain/bear in their biochemical structure the point-mutations (PM) of the following, to come, HAART-x regimen), and which manage to completely hinder and prevent the emergence of HAART-x resistant HIV-1 should be included as components of the (therapeutic) vaccine, (Vaccine-x). We also believe that each point-mutation (PM-x) should be present on a separate DNA-sequence, and the optimal proportion of DNA-sequences bearing the various point-mutations(PM-x) should be found experimentally.

However, DNA-sequences of HIV-1 which bear all point mutations (PM-x) of the following HAART-x regimen should also be tested and evaluated. Even more, whole killed (or highly inactivated) HIV-1 virus bearing all the point mutations (PM-x) of the following HAART-x regimen should also be tested as a potential component of the (therapeutic) vaccine, (Vaccine-x).

The presently existing Remune vaccine (HIV-1 Immunogen, Salk vaccine, or AG1661) developed by the Immune Response Corporation should also be modified and tested for its potential usefulness as an anti-HIV-1 vaccine or anti-HIV-1 therapeutic vaccine to be used as the (Vaccine-x) component in (Vaccine-x, HAART-x) -couples. Remune is made from whole HIV particles, which have had their envelope layer stripped off and have been made harmless by radiation and chemical sterilization, and are mixed with incomplete Freund's adjuvant in the final formulation.

An ideal anti-HIV-1 therapeutic vaccine (IdealVaccine-x), to be used in (Vaccine-x, HAART-x) -couples or (Vaccine-x, MegaHAART-x) -couples, should have the capacity to prevent the emergence of any HAART-x resistant or MegaHAART-x resistant HIV-1 virus, so that the series of HAART-x and MegaHAART-x regimens can progressively reduce HIV-1 viral load to zero, and thus eliminate HIV-1. In other words (IdealVaccine-x) should be able to prevent the emergence of any point mutation and the emergence of any resistance-mutations-pattern for all antiretroviral drugs and for all their combinations, and should contain all possible HIV-1 mutations, and transfer them to the immune system. Apparently, the human immune system has the capacity to develop immune responses against a practically unlimited number of pathogens, when it is warned in advance by vaccines.

DISCUSSION

This entirely new approach to treat HIV-1 infections with a succession of (Vaccine-x, HAART-x) -couples or (Vaccine-x, MegaHAART-x) -couples, can be adapted and used to treat all possible hard - to - treat infectious diseases against which at least one effective (or at least mutation-inducing) drug exists, and it can ultimately lead to the eradication of many highly pathogenic bacteria, fungi and viruses which are already resistant to presently available drugs..

Especially hard- to- treat infectious diseases, tuberculosis (TB) , malaria , sexually transmitted diseases (STD), may be cured and eradicated, and the emergence of new drug-resistant pathogens may be prevented, when (Vaccine-x, Drug-x)-couples are carefully selected, and when they are used wisely and rationally .

(Vaccine-x, Drug-x)-couples may also be used in the treatment of cancer ($_9$) where the role of the therapeutic vaccine (Vaccine-x) can be taken either by killed cancer cells bearing on their DNA the resistance - mutations - pattern (RMP) that would be induced into the cancer cells by the anti-cancer drugs to be used in subsequent, following chemotherapy, or by small DNA-sequences which contain the resistance - mutations - pattern (RMP) that would be induced into the cancer cells by the anti-cancer drugs to be used in subsequent, following chemotherapy, or by both.

CONCLUSIONS

HIV-1 can be be eliminated from the human body, by treatment with successive (Vaccine-x, HAART-x)-couples, followed by (Vaccine-x, Mega-HAART-x)-couples.

(Vaccine-x, HAART-x)-couples are the symbol and expression of how the antiretroviral treatment can be synergetically coordinated with the human immune system in order to eliminate HIV-1 from the human body and thus eradicate HIV-1 and cure AIDS.

An entire new industry of multivalent therapeutic vaccines (MTV-x), polyvalent therapeutic vaccines (PTV-x), and even multivalent-polyvalent-therapeutic-vaccines (MPTV-x) against HIV-1 should/will emerge after the publication of this article, and these therapeutic vaccines against HIV-1, all termed as (Vaccine-x) in this article, should be used together with their corresponding HAART-x or Mega-HAART-x regimens, in (Vaccine-x , HAART-x)-couples, or (Vaccine-x , Mega-HAART-x)-couples respectively, to eradicate HIV-1 and to cure AIDS.

The Authors of this article believe that an entire industry of standardized multivalent, polyvalent, and even standardized-multivalent-polyvalent-therapeutic-vaccines (SMPTV) will emerge, to act complementary and synergistically with all types of HAART-x regimens (or even Mega-HAART-x regimens) in order to eradicate HIV-1.The design and production of (Vaccine-x , HAART-x)-couples and of (Vaccine-x , Mega-HAART-x)-couples may also unify and integrate the Pharmaceutical Industry, the Vaccine Industry, and the Biochips Industry and (Vaccine-x , Drug-x)-couples may be developed for the treatment and cure of HIV-1/AIDS, of all other infectious diseases, and of cancer ($_9$).

References

1. Hahn BH, Robertson DL, McCutchan FE, Sharp PM , Recombination and diversity of HIV: implications for vaccine development, Neuvieme Colloque Des Cent Gardes, 1994, 87-94;
2. Robertson DL, Sharp PM, McCutchan FE, Hahn BH, Recombination in HIV-1, Nature 1995, 374, 124-126;
3. Robertson DL, Hahn BH,Sharp PM, Recombination in AIDS viruses, J.Mol.Evolution , 1995, 40, 249-259;
4. Sharp PM, Robertson DL, Hahn BH, Cross - species transmission and recombination of 'AIDS viruses, Phil. Trans. R. Soc., London B, 1995,349 : 41-47;
5. Kalish ML et al, Recombinant Viruses and Early Global HIV-1 Epidemic, Emerging Infectious Diseases, Vol.10, No.7, July 2004;
6. Secasan I, Pop DI , Fighting HIV with HIV, Medical Hypotheses, 1998 Jan;50(1):39-42;
7. Kinloch-de Loes S, Autran B: HIV-1 Therapeutic Vaccines, J Infect 2002 ; 44 : 152-159;
8. Kinloch-de Loes S: Role of therapeutic vaccines in the control of HIV-1, J Antimicrob Chemother., (2004) 53, 562-566;
9. Secasan I, Pop DI, Secasan CC, Potentially New And Innovative Treatments For Superficial, Muscle-Invasive, And Metastatic Transitional Cell Carcinoma (TCC) Of The Bladder , The Internet Journal of Oncology, 2005, Volume 2, Number 2;

Author Information

Iosif Secasan
Department of Urologic Surgery, Spitalul Judetean Resita / The Hospital of Resita

Dan I. Pop
Data International SRL

Ciprian C. Secasan
Department of Microbiology / Department of Urologic Surgery, Spitalul Judetean Resita / The Hospital of Resita