There are no translations available.

C.82bis- Therapeutic Protocol defended by the "POSITIFS" Association. Replacement of HAART by a low toxicity treatment involving new targets of HIV, in patients intolerant to protease inhibitors or resistant to anti-integrase or seeking a less toxic treatment

Introduction

Although the main objective of zero or undetectable viral load is achieved by a treatment based on protease inhibitors and / or anti-integrase, demonstrating their effectiveness, these treatments are still imperfect because of their toxicity and side effects resulting from these two options:
1) Lipodystrophy, for anti-proteases, threatening the long-term development of cardiovascular complications and increased mortality risk significantly, or
2) ineffectiveness of anti-integrase
and forcing them to ascertain whether there is another possible treatment option, but that it must be found, in the case of former patients who have exhausted all the "arms" of the armamentarium of Pharmaceutical Companies.

The absence of alternative therapeutic option in these two impasses is especially urgent the discovery of new efficient and especially non-toxic treatments that can take over in case of major side effects (lipodystrophy). Ideally, a completely harmless armamentorium, since the patient must undergo treatment for life, and who nonetheless remain 100% effective, that is to say capable of maintaining an undetectable viral load: An ideal treatment.

Basis of the proposal of clinical research protocol:

A) Biological Requirements

1) work of Bandivdekar on **Mannose receptor** and Tran GMK work on **sodium channel voltage-dependent** ,
both co-receptors for HIV non-target date by Pharmaceutical Companies.
The mechanism of action at the molecular biology is blocking the virus at the entry into the cell, by targeting these two new receptors (different from CD4, CCR5 and CXCR4):

a) The mannose receptor and
b) The receptor whose ligands are gp120, gp41, Nef and part scorpion-like protease (Tran GMK, work submitted, not yet published), this receptor is the sodium channel voltage-dependent or receptor long scorpion venom toxin.

Blocking the sodium channel was already successfully completed and published (Fredj and Dietlin, society Newpharm) in 1989, clinically with Tacrine (tetrahydroaminoacridine or THA), which acts specifically on the sodium channel (Schauf and Sattin), but hepatotoxicity of Tacrine had prevented the increase in dose until the optimal dose (ie beyond 150 mg / day), resulting in a modest effect if real and an obligation to properly navigate the pitfalls of hypertransaminémia. The first test with Tacrine on a series of only a few patients had used doses too low (test of English Mike Youle) and was quickly abandoned.

This concept of the scorpion venom toxin model was developed from 1988-1989 by Tran MKG and also simultaneously by Werner in Germany (published in AIDS, see Garry RF editorial citing, with my permission, my alignments) . The European AIDS Clinical Society (EACS) was also elected as a member of its Scientific Council for about 10 years, Tran GMK for his decisive contribution to this discovery while to actually innovative, but considered a little "magic "for the time. It must be said that at the time, astrologers claimed that the AIDS epidemic had become following the merger of Pluto (planet of Scorpio) Earth (see Daily Doctor). They also predicted that the epidemic would decline gradually as and when the distance of Pluto, which ... has been achieved.

This closed unscientific astrological parenthesis, it is the work of very pure molecular biology have revealed very highly significant molecular mimicry between the scorpion toxin and HIV-1. This is not an astrological demonstration based on "influence" of Pluto on Earth.

A poisonous toxin is a molecular mimic virus has already demonstrated in the case of rabies and snake neurotoxin Naja (Lentz, Science). There is nothing there astrological, it's totally simple scientific toxinology. Still regarding rabies, we confirmed the presence of a second snake neurotoxin at residue Arg 333 (Tran GMK, unpublished), thus explaining the two clinical forms of rabies.

Confirmation of the concept of scorpion toxin by the Thai RV144 vaccine

This vaccine provides a low final protection of about 30%, but mainly evident at the beginning of the test (probably because HIV-1 has not yet had time to mutate): Statistically, the 30% protection was questioned later, however, the fact remains that the difference is very significant at the beginning of the trial, with significantly more than 30% protection.

Recently, therefore, there has been an unexpected confirmation of the concept of voltage-gated sodium channel and toxins binding to the channel, the scorpion toxin: In fact, the first anti-AIDS vaccine in the world have had an efficiency (. Rerks-Ngarm S et al, NEJM, 2009) after more than a hundred failures, the recent Thai RV144 vaccine is - we now know - by an immunological mechanism targeting precisely, and only, the V1 and V2 loops of the gp120 of the envelope of HIV-1;

The correlate of vaccine protection is humoral: neutralizing antibody loops V1 and V2.

But these two hypervariable loops are well known by TRAN GMK, who had studied under the scorpion toxin, as well as the V3 loop (TRAN GMK): This work is not yet published, but V1 and V2 are also cone sea toxins (for the Thai vaccine strain) and scorpion (for the MN strain). This discovery was made in 1994 for the MN strain, but its meaning at the time was only to reinforce the concept of scorpion toxin obtained with mimicry between V3 and scorpion venom of Androctonus Australis Hector Aah II that Marc Girard had confirmed on the animal discovering that anti-V3 antibodies protected chimpanzees, though specific type only.

Now, the success of the RV144 Thai vaccine, UNDISPUTED AT THE BEGINNING, however modest or no in the end, allows to suggest that the protection afforded to a clear mechanism: Neutralization of V1 and V2 loops of antibodies. One knows the type of immunity: Humoral alone, without the intervention of cellular immunity, especially the target antibodies are precisely known: the V1 and V2 loops of the gp120 envelope of HIV-1. Therefore, as these loops are cone sea and scorpion toxins, that means they bind to the voltage-gated sodium channel that is the receptor of two toxins, both the toxin of the cone and the toxin long of the scorpion.

In short, to sum up, one of the "correlates of protection", so mysterious and so sought in vain for decades, in the anti-AIDS vaccine is an antibody binding to the hypervariable loops V1 and V2 gp120, and these two loops are toxins cone sea (for the Thai vaccine strain) and scorpion (for the MN strain) binding to the sodium channel. This channel is the therapeutic target of omega-3. (Isbilan Banu 2006 Marchioli R 2002 study Gissi).

Give omega 3 leads to inhibit V1, V2 and V3 loops of gp120 and gp41 of HIV-1.

2) Work on **Resveratrol**
Zhang HS (anti-Tat activity) of
Heredia (synergy with nucleoside analogues) and
Tran GMK (anti-Nef activity, results presented at the 17th Post ISHEID Marseille and on www.positifs.org C77). Nef acts on the CD4 count, the CD4/CD8 ratio and as Nef represents 85% of the mRNA of a person infected with HIV-1 cell, on the other hand is a "superantigen" (which amplifies 10 000 times the action of the virus), inhibit Nef will be crucial to overcome AIDS.

Anti-Nuclear Factor kappa B activity (NFkB) of resveratrol suggests it will have a preventive effect on the occurrence of cancer, which is a sword of Damocles over the long term AIDS patients. Among other anti-NF- kB there is turmeric, Epi gallo catechin-3-gallate (EGCG) in green tea. So these are anti-cancer drugs, but also simultaneously anti-Nef. Their use is a double benefit for the patient: Prevent HIV-1 to act, particularly increasing the rate of CD4 (since Nef decreases the rate) and prevent the occurrence of cancer.

This is not mere speculation of a molecular biologist locked in his ivory tower, but a clinic is authenticated by clinical studies published in the international literature: The anti-NF-kB molecules such as green tea (EGCG) have been studied in lung cancer of smokers in January 2009 on 700 smokers Coronado (USA): EGCG reduces the risk 15 times. Similarly, the fungi associated with green tea reduced by 85% the risk of breast cancer in a 2009 study involving 1,000women.

About lung cancer, AIDS as it affects the rest of the population, and therefore the interest of EGCG is major. This suggests that we should study the incidence of cancer as "end point" in AIDS patients taking anti-NF-kB, to determine whether a cancer preventive effect.

IN SUMMARY

The attack HIV-1 virus is a crossfire (as in defenses Vauban fortifications): The abuser HIV-1 is subjected to heavy fire from four different directions simultaneously attack is:
-gp120(theD-Mannose)
-Nef and Tat (by resveratrol)
-Reverse Transcriptase (with 3TC) and
-envelope glycoprotein (gp120, gp41) (for the omega-3).
Note that the Omegaven is an IV infusion of omega-3, used in parenteral lipid diet.

Clinical confirmation

1) In addition to the former work Fredj G and Dietlin in 1989 on the inhibition at the sodium channel (the Tacrine)

2) Results of one of us (Adrien Caprani) with combination therapy (3TC, Resveratrol, D-Mannose, Omacor) Poster presented in the 17th ISHEID Marseille (C75 and C75bis on www.postifs.org) . This treatment alone can maintain an undetectable viral load for 10 months, no significant changes in CD4 (504 + / -15 vs. 492 + / -30) *, with a slight increased CD4/CD8 ratio (0.61 vs. 0.50), normalization of activated T (7% vs. 15%) and a significant increase in natural killer (NK) cells (24% v 8%).
* NB The last digit of CD4 is very favorable, with a climb of about 700 to ~ 550-600 (August 2012). The "stall" ascending was not known and had not been published at the time of ISHEID Conference in Marseille.
2) The objective, given the upward momentum of CD4 would get 300 more CD4 or CD4 in 1000, or normal count, that is to say, the complete recovery of the patient, improving the current treatment in August 2012 by several complementary therapies;
A more powerful protocol theoretically include, in addition to four other (3TC + Resveratrol + D-Mannose + Omega-3) harmless nutraceuticals part somehow the daily diet.

3) 4 nutraceuticals are possible:
- Green tea (EGCG), anti-NF-kB
- A spice, turmeric (anti-integrase), which is not properly absorbed if not associated with black pepper (WARNING!)
- Traditional African Herbal Medicine: Herbal Alternanthera pungens (Djohan YF, 2009, Ann

Biol Clin 67: 563-8)
- TRIPHALA MIX (containing Arura) Tibeto-Ayurvedic (TRAN GMK, unpublished)

A fifth-requires prior virologic study to test SPECIFICALLY against HIV-1: The grapefruit seed extract (about 800 active pathogens: viruses, bacteria and fungi).
One-sixth candidate is sodium salicylate, anti-NF-kB, which inhibits HIV-1. A derivative of the second generation was recently synthesized in the U.S. to avoid side effects.

CRITERIA FOR INCLUSION:

Patients intolerant to protease inhibitors and / or non-responders to anti-integrase.
Patients responding to standard treatment with undetectable viral load.

Absence of the 184 mutation in reverse transcriptase (3TC resistance mutation)

Number of participants: 300 in three groups of 100 patients

Test duration: 1 year

Treatment groups:
First and second groups: 100 patients intolerant to protease inhibitors (group 1) and
100 patients intolerant / RESISTANT anti-integrase (second group)

Combined therapy
3TC (150 mg 2/day in 2 doses) +
Resveratrol | Biotivia Transmax TR (500 mg 2/day in 2 doses)]
D-Mannose (3g/day in 3 doses)
Omega-3 [Omacor (2g/day in 2 doses)]
for two types of patients

3rd group: conventional treatment with drugs first line or second line until an undetectable viral load, and when it is achieved, immediate replacement with 3TC + Resveratrol + D-Mannose + Omacor (n = 100 patients responding to standard therapy with undetectable viral load) to prevent the occurrence of side effects.

Patient monitoring
CD4 and CD4/CD8 ratio, viral load + standard blood parameters at 1 month, 3 months, 6 months, 12 months
Activated T cells and natural killer (NK) at 0, 6 months, 12 months

Evaluation of the protocol and expected results for the-3 treatment groups:

Group 1: For patients unresponsive to standard treatments, maintaining undetectable viral load and maintaining or increasing CD4
Groups 2 and 3: For patients intolerant to protease inhibitors and / or anti-integrase return to undetectable and increased CD4.
Disappearance of lipodystrophy in group 2 (after stopping protease inhibitors)
Absence or decrease the severity of the cancer or cancer risk in the 3 groups.

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