There are no translations available.

C.85-Thai AIDS Vaccine RV 144: Molecular Homology Between HIV-1 Gp 120 Envelope First Conserved Region C1, Which Induces IgA Antibodies Increasing AIDS Risk, And The Complement Receptor CR1

Thailand RV 144 vaccine, despite gp120 V1/V2 loops neutralizing IgG, has a low 31% efficacy, mitigated by IgA antibodies against the first conserved region C1 (odds ratio 3.15) *(Haynes BF, 2012)* . We analyse the biological significance of C1 by

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rotein (BLASTP) and visual Amino Acid (AA) sequences comparison: We screened C1 of the vaccine 2 Thailand strains and all HIV-1 strains (HIV Sequence Compendium 2012 Kuiken C, Los Alamos) on Homo Sapiens and found a molecular homology between C1 (AA 112-122) and

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eceptor type 1 CR1 (CD35) isoform S (AA 2089-2099), in the CCP 32 [NP_000642]; the corresponding numbering of allotype F is AA 1639-1649, in the Sushi 25 [P17927]:

C1 112-**WDQSL KP CVKL**-122
C1 (strain CRF 37_cpx) *(Powell RL, 2007)* 112-**WGPKL KP CVKL**-122
CR1 isoform S CCP 32 2089-**WGPKL**(**H,P**)**CS RV**-2099

Domain structure of human complement receptor CR1 and its most common cell expression profile. Human CR1 F allotype contains 30 Short Consensus Repeats (SCRs), each depicted by spheres. Indicated in **red** are the SCRs mediating binding to the C3b fragment (*Hea JQ, 2008).*

The tip of the complement receptor CR1 loop (Proline P2095) is read *in retro inverso* : 2096-(H,P)-2095, instead of 2095-PH-2096.

Such **tip inversion** exists: Epidermal Growth Factor (EGF) and Transforming Growth Factor-alpha (TGF-a) bind to the same EGF Receptor, despite different tip linear sequence, but in 3D have superimposed loop tip AAs (E and V):

Rat EGF 24 - **E S V** - 26

TGF-alpha 26 -(**E,Q**,**V**)- 24

Anti-C1 IgA harmfulness is explained by *Wagner C (2006)*: Anti-complement receptor CR1 antibodies profoundly inhibit T cell proliferation by inhibiting Interleukin-2 (IL-2)/Interferon-gamma synthesis and IL-2 efficacy, explaining IL-2 clinical trials failure despite T4 cell rise *(Pett SL, 2010)*. CR1 is decreased in lung tuberculosis *(Senbagavalli P, 2008).*

It acts on macrophages and dendritic cells.

Conclusion

An AIDS vaccine must avoid anti-C1 IgA antibodies, because C1 is a molecular mimetic of CR1 and therefore the cross-reactive anti-C1 IgA are anti-CR1 auto-antibodies which profoundly inhibit T cell proliferation. These auto-antibodies could also promote lung tuberculosis. We advocate an AIDS vaccine devoid of this envelope gp120 first constant region C1 deleterious epitope to ameliorate the 31% efficacy observed with the Thai RV 144 vaccine.

An AIDS therapeutic vaccine (as was the case for Pasteur anti-rabies vaccine) would be more rapid to develop, step by step, than a classical prophylactic vaccine: The rapidity of a therapeutic vaccine is calculated in months, whereas for a prophylactic vaccine, each trial would take dozen of years. The same therapeutic vaccine, when finally successful, can be then converted in a prophylactic vaccine (following the anti-rabies vaccine example).

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