C.81-Voltage-gated sodium Na+ channel allostery as the basis for the scorpion venom model of AIDS:Molecular homology between between spider toxin and HIV-2, and scorpion toxin and HIV-1 envelope gp41 sequence SWSNKS

Abstract accepté pour EMBO Conference on Allosteric interactions in cell signaling and regulation(Institut Pasteur Paris,May 14-17, 2013)

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Objective : Allosteric differences explain why spider Atrax toxin differs slightly from scorpion Androctonus AaH2, despite the fact they bind to the same Na+ channel receptor site 3 (Little MJ, 1998). We found a molecular mimicry between HIV-1 envelope gp 120 V3 and V2 loops, but nothing between scorpion and HIV-2, which is less virulent than HIV-1.

Methods : Amino acid and three-dimensional (3D) structure (Pallaghy PK, 1997) comparison between

HIV-2/SIV and the arthropod family, conotoxin and sea anemone toxin, all ligands of the Na+ channel.

Results : 1°) There is a match between lethal Australian spider Atrax Robustus toxin and HIV-2, but only in 3D, although the structures differed: Spider key residues (4-KR-5/M18/K19/Y22/23-AWY-25/Q27/C31) superimpose on HIV-2 residues (180-KK-181/M172/K173/Y183/186-AWY-188/Q190/C194).

2°) We confirm the scorpion model of HIV-1, by aligning scorpion toxin COOH-terminus with

HIV-1/chimpanzee CPZ.CD90.ANT gp41 sequence SWSNKS, or 3S, a potential therapeutic AIDS vaccine (Vieillard V, 2008).WSNKS is deleted in HIV-2/SIV-AGM (explaining why African Green Monkey AGM don't get sick):

scorpion chimera C...KLAC.CY-SVP-WNPTWS-RSNTCGKK-carboxy-terminus

HIV-1/SIVchimp C.. -KLV..CYTSVPDWVPSWSNKSQTCAKN

Conclusions : Na+ channel has many sites, the site 3 binding scorpion and spider toxins, namely respectively HIV-1 and HIV-2 envelope; their different degree of virulence is explained by the different allosteric modifications between scorpion and spider toxins. Another implication is to ameliorate the clinical results obtained with a Na+ channel ligand, omega 3, which is effective and non toxic in AIDS treatment. By combining many ligands