

**Highly pathogenic Influenza virus A H5N1 Vietnam Hemagglutinin (HA2) contains a scorpion alpha-toxin. Sodium channel inhibitors as therapy.**

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Guy Mong Ky Tran(1) & Adrien Caprani(2)

(1) Retired since 2014 from University of Auvergne Rhone-Alpes, Health Regional Agency, Public Health Department, Hospital Hotel-Dieu, Clermont-Ferrand ; 31 Av du Bois - Chatenay Malabry, France. email: [mkg\\_tran@yahoo.fr](mailto:mkg_tran@yahoo.fr)

(2) Association "Positifs", 147 chemin de la futaie, 83550 Vidauban, email: [positifpresident@yahoo.fr](mailto:positifpresident@yahoo.fr)

During the Influenza H1N1 pandemic, we found in Influenza virus A H1N1 Japan Hemagglutinin (HA1) 246-YFWKLV-251 the active site loop 39-YFWKLA-44 of the scorpion toxin AaHIT4 (Tran GMK, ISHEID Conf, Toulon, France, 2010: 0291 . [www.Positifs.org](http://www.Positifs.org)), with the surprising discovery of a RETRO-INVERSO lecture (from COOH- to NH2-terminus) of Influenza virus HA2 466-VKEYL-462 (= HA2 122-118) matching with the crucial NH2-terminus active site of scorpion 1-VKEgYL-6 which induces broadly cross-reactive neutralising antibodies (Devaux C, 1996). We developed further this short retro-inverso lecture and found a complete scorpion alpha-toxin in the highly pathogenic Influenza virus H5N1 Vietnam 1203/2004 HA2 : Influenzavirus(retro-inverso)126-LQLRVKD-Y-LNKVNSD- -HFD-LT R- ENEMLV-100

## C.112-Highly pathogenic Influenza virus A H5N1 Vietnam Hemagglutinin (HA2) contains a scorpion alpha

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Scorpion Bot9/AaH2/CsE1 -4 -AEIKVKDgYIVNKNVSDgcKYDcL(L,K)gENEFCL- 26

Influenza virus A H5N1

78-ENLNK K M ED-GFLDV W TY- NA-96

Scorpion Bot3/AaHP985

24-EECNK(K,L)gDsGYCD(I,W)TYgDA-44

Influenza virus A

45-IDgVPNKVNSI-55

62-QFE(V,A)GR-EF-70

Scorpion Bot2/AaH2/LqqV 49-ID-LPDKVRTI-58 Bot2/BotXI 58-RI EV AGRcHF-65

All the scorpion active site residues K2, Y5, V10, Y14, W38 & G61-R62 (AaH2

numbering) matched with Influenza K121, Y119, V115, F110, W92 & G67-R68.

This was very surprising, because Influenza HA2 (45-126) has no cysteine. Many scorpion cysteines (C16, C26, C36) were matched with Influenza Leucines (L108, L80, L89) or gapped (C12, C63). In conclusion, avian Influenza virus A H5N1 HA2 contains a complete scorpion alpha-toxin, but devoid of any cysteine core structure; this means that its receptor is a sodium Na<sup>+</sup> voltage-gated channel and consequently Influenza virus can be inhibited by Na<sup>+</sup> channel modifiers (vitamin B1, vegetal fatty acid omega-3, antiarrhythmics, local anaesthetics (procaïne), eugenol, antimalarials (quinine), antiepileptics). Conversely, fatty acid omega-6 are deleterious. For Influenza vaccine, the epitope mimicking the scorpion NH<sub>2</sub>-terminus seems crucial. This data points to the importance of RETRO-INVERSO lecture (for instance, the RGD adhesion motif) in deciphering protein function. Three homologies of H5N1 with platelet Integrin ITGB3, disintegrin ITGA2b and plasminogen activator explain the hemorrhagic character of avian Influenza.

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