There are no translations available.

Highly pathogenic Influenza virus A H5N1 Indonesia & Vietnam Hemagglutinin (HA1) contains an urokinase-plasminogen activator explaining the fibrinolysis

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Avian Influenza is compared to a chicken lethal Ebola for its internal hemorrhagic symptoms. Oseltamivir is inefficient and not recommanded in hemorragic influenza. In 1996, Zhilinskaia IN (Vopr Virusol) found by computer analysis a similarity between Influenza virus hemagglutinin HA and plasminogen activator (PA), explaining the fibrinolysis. We analysed further these results in Influenza virus A H5N1 Indonesia (83% mortality) and Vietnam HA1. We compared to urokinase (U-PA), tissue PA, TSV-PA, Batroxobin. Results : All the 3 active site residues of serine protease (His, Asp, Ser) were found and the best match was with U-PA :

H5N1 Indonesia/Vietnam IPKSS-W--S-SH

U-PA/t-PA active site His ILISScWviSaTH

H5N1 Indonesia/Vietnam G I HHpNDAAEQTK

U-PA/t-PA active site Asp (A,L)HH NDI ALQ IR

H5N1 Vietnam KGDS- - TIMKS(L,E)EYGNCNTKCQTPMGA I

U-PA/t-PA active site Ser QGDSggPLVcS L Q WIRSHTKGEE- NG(A,L)

H5N1 Indonesia/Vietnam 141-YLGKSSF(R,F)N-150

U-PA YLGR-S(L,R)L N

Conversely, Influenza H7 China HA1 has His replaced by Arg, Asp replaced by Ser. The motif His-Phe (HF), in the pocket binding Plasminogen clivage site Arg-Ala-Arg, was present in Influenza H5N1 and U-PA (319-HF-320); but not in Influenza virus H7 China, replaced by Gly-Gly (inactive). Conclusion : The plasminogen activator in avian Influenza virus H5N1 hemagglutinin HA1 (Zhilinskaia) was confirmed and may explain fibrinolysis in hemorrhagic Influenza. It seems rationale to use plasminogen inhibitors to block this fibrinolysis. A peptidomimetic drug of the plasminogen Arg-Ala-Arg (RAR) at the cleavage site Arg / Ala can be designed by docking. This strategy was successful in HIV-1 tritherapy, with FP peptidomimetics.