Turkish Journal of Veterinary & Animal Sciences

Volume 33 | Number 5 Article 11

1-1-2009

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TÜBİTAK

Short Communication

Turk. J. Vet. Anim. Sci.
2009; 33(5): 437-438
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doi:10.3906/vet-0803-32

Structural aberration in HA associated with adaptation of human influenza A H3N2 virus in embryonated chicken eggs

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Received: 25.03.2008

Abstract: Molecular changes associated with adaptation of human influenza A virus in embryonated chicken eggs are reported: 4 amino acid substitutions occurred in HA (G186V, S219F, V226I, V309I). These substitutions allowed binding to SAalpha2,3Gal- and SAalpha2,6Gal-containing receptors, conferred SAalpha2,3Gal specificity, and preserved antigenicity. Here, the author reports the result of protein secondary structure predictions of the adaption from its primary sequence using the NNPREDICT server. Comparing the classical HA of H3N2, the adaptation has additional helices and strands and these identified structural changes should be the explanation for the reported binding and antigenicity changes.

Key words: Adaptation, H3N2, HA, structure

Avian flu or bird flu, caused by an atypical avian influenza virus (HxNx virus), is a new emerging infectious disease worldwide. According to the recent study by Widjaja et al. (1), molecular changes associated with adaptation of human influenza A virus in embryonated chicken eggs were evidenced and 4 amino acid substitutions were detected in HA (G186V, S219F, V226I, V309I). Widjaja et al. (1) stated that these specific substitutions allowed binding to SAalpha2,3Gal- and SAalpha2,6Gal-containing receptors, conferred SAalpha2,3Gal specificity, and preserved antigenicity. Here, the author reports the result of protein secondary structure predictions of the adaption from its primary sequence using a new computational bioinformatic tool.

For data mining, the database PubMed was used for searching or mining of the amino acid sequence for HA of H3N2. Then the specific mutation as already described in adaptation was experimentally performed. The author performed further protein secondary structure predictions of classical and adaptation of HA of H3N2 from its primary sequence using the NNPREDICT server (2). The resulted calculated secondary structures were presented and compared. Comparing the classical HA of H3N2, the adaptation has additional helices and strands as presented in the Figure.

A potential source of H5N1 viral infection is contamination of inside avian eggs through intra-

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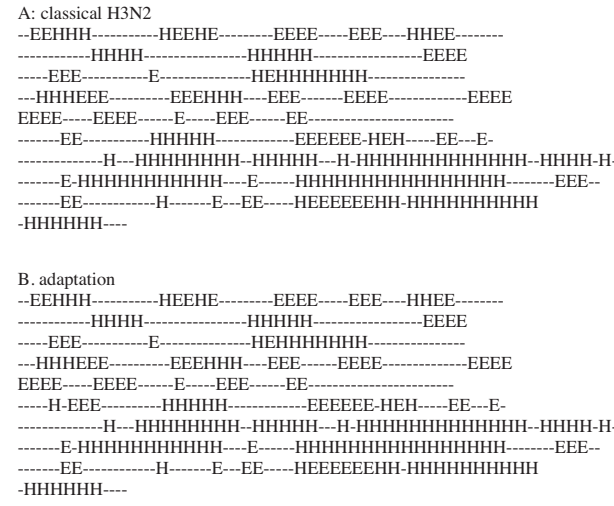

Figure. Predicted secondary structure of HA of classical H3N2 and its adaptation *(H = helix, E = strand, - = no prediction).*

uterine transmission (3). Hence, the study of the specific adaptation of the virus in embryonated chicken eggs is useful. However, there are only a few reports on this topic. Recently, the adaptation of H3N2, a type of avian flu, is noted. Although the mutations are already documented there is no further additional clarification on the affected molecular structure.

In this brief report, the author predicted the secondary structural change within HA of H3N2 owing to adaptation and these identified structural changes are the probable explanation for the reported binding and antigenicity changes (1). Indeed, it was evidenced that the passing of H3N2 virus in embryonated eggs might bring about the adaptation and selection of variants demonstrating significantly decreased pathogenicity and neurovirulence in mice that appeared to be attributable to some specific amino acid changes in the HA as well as internal proteins (4). Of interest, although there are some reports on some mutations within HA of avian flu there is no further clarification on any affected molecular structures. The study on the molecular structure of mutated virus particle is useful for a better understanding of the molecular pathogenesis of atypical bird flu in humans.

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