A MINIMAL STRUCTURAL REQUIREMENT FOR PROTEOLYTIC CLEAVABILITY OF HA AND FOR PATHOGENICITY OF AVIAN INFLUENZA VIRUSES

143

F. BOSCH, M. ORLICH, B. GIESENDORF, and R.ROTT
Institut für Virologie, Justus-Liebig-Universität Giessen, Frankfurter Strasse 107, D-6300 Giessen, FRG

The nucleotide sequences of the connecting peptide regions on the HA of pathogenic avian strain A/fowl/Victoria/75 and of three variant strains were determined by dideoxy sequencing of reverse transcripts of virion RNA primed with synthetic oligonucleotides. The deduced amino acid sequence of the connecting peptide of the "wild type" HA is Lys-Lys-Arg-Glu-Lys-Arg-Gly (with Gly representing the NH_2-terminal residue of the HA_2 subunit). All three variant strains, obtained by diluted serial passages in chicken embryo cells (CEC), showed the same single base change in the connecting peptide. The resulting amino acid change, which was unexpectedly located C-terminal to Glu, rendered the HA of the variants noncleavable in infected CEC and the viruses were no longer pathogenic for chickens. The biochemical/biological implications of these results are discussed.

THE ROLE OF SPECIFIC GENES FROM COLD-ADAPTED INFLUENZA A AND B "MASTER" STRAINS IN CONFERRING PHENOTYPIC AND GENETIC MARKERS OF ATTENUATION TO CANDIDATE VACCINE REASSORTANTS.

144

H.F. MAASSAB, D.C. DEBORDE, A.M. DONABEDIAN, T. ODAGIRI, M.H. SNYDER AND B.R. MURPHY, Dept. of Epid., School of Public Health, 109 Observatory, Univ. of Michigan, Ann Arbor, MI. 48109 and NIAID

The contributions of specific genes derived from attenuated and cold-adapted (ca) "Master" strains were studied for pathogenicity, temperature - sensitivity, (ts) and cold-adapted (ca) phenotype. These phenotypes were analyzed by examination of reassortants containing single, double and triple genes derived from the ts and ca donor lines. Single gene reassortants for type A influenza viruses were not ca or ts and had no evidence of decreased virulence. However, all single gene reassortants of type B influenza viruses tested were ca and not ts, with the exception of the single gene reassortant inheriting RNA3 which was both ca and ts. Reassortants inheriting two genes showed some decrease in virulence, they were ca but not ts, and the triple gene reassortant had a level of attenuation comparable to influenza live vaccine candidates and the cold-adapted donor strains.