S49-3 Function of pandemic influenza virus neuraminidase

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N2 neuraminidase (NA) genes of the 1957 and 1968 pandemic influenza virus strains possessed avian-like low-pH stability of sialidase activity, unlike most epidemic strains. The NA genes of H3N2 viruses isolated from 1971 to 1982 had evolved from the side branches of NA genes of H2N2 epidemic strains isolated in 1968 that were characterized by the low-pH-unstable NA, though the NA genes of the 1968 pandemic strains preserved the low-pH-stable NA. These findings suggest that the prototype of the H3N2 epidemic influenza strains isolated after 1968 probably acquired the NA gene from the H2N2 low-pH-unstable NA strain by second genetic reassortment in humans. We found that the virus bearing the low-pH-stable NA and sialidase activity in late endosome/lysosome traffic enhance virus replication. We also found that two amino acid substitutions in the low-pH-stable A/Hong Kong/1/68 (H3N2) NA and a single substitution in the low-pH-unstable A/Texas/68 (H2N2) NA resulted in significant change in low-pH stability. Here we show that N1 NA of the “Spanish” pandemic influenza virus in 1918 has the avian-like low-pH stability of sialidase activity, which maintains in N2 NAs of all human pandemic viruses in 1957 and 1968. We determined NA amino acid residues responsible for the low-pH stability of the 1918 virus. Acquisition of low-pH stability from the low-pH-unstable N1 NA by mutation enhances virus replication. The low-pH stability of influenza virus NA contributes to virus replication and pandemic. It may be helpful in development of new therapy for influenza virus and pandemic prediction.