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## Role of a New RNA Species in H5 Influenza A Pathogenesis

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Influenza A virus is an important human and animal pathogen that causes devastating disease and economic losses. There are many subtypes of influenza A virus and the subtype is determined by viral surface glycoproteins known as Hemagglutinin (HA, H1-H16) and Neuraminidase (NA, N1-N9). Two subtypes (H1N1 & H3N2) are currently circulating amongst humans and all HA and NA subtypes have been detected in avian species (e.g. water fowl). Some H5 and H7 avian viruses are highly pathogenic and avian viruses occasionally cross the species barrier and infect humans. A new H5N1 strain emerged in birds in 2003. H5N1 viruses have caused 372 documented zoonotic infections, which have resulted in 235 deaths. The H5N1 strain is a pandemic threat and it is imperative that molecular mechanisms involved in interspecies transmission and pathogenesis of influenza A viruses continue to be elucidated. We have discovered a new viral RNA species expressed in cells infected by another highly pathogenic H5 virus. This RNA species is a 3' subgenomic fragment of the H5 gene segment. Our hypothesis is that the subgenomic HA RNA is generated by the recognition of a novel internal promoter element. We are developing a reverse genetics system to genetically manipulate this H5 strain so that we can examine how mutations in the putative internal promoter influence subgenomic H5 RNA/protein production, and determine this has an effect on the virus phenotype in vitro and in vivo. This research may discover a new mechanism employed by highly pathogenic influenza viruses.