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Pathogenesis of the Adapted A(H1N1)pdm09 Influenza Viruses in different organs of infected Mice

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Pandemic A (H1N1) pdm09 virus has caused substantial morbidity and mortality globally and continues to circulate, which may lead to an increase the pathogenic features of viruses by adaptation to the human. To address this problem, we studied changes of biological properties of the pandemic viruses during adaptation to experimental mammals and analyzed cellular localization of positive-stranded A(H1N1)pdm09 RNA in the inner organs of infected mice. To increase the virulence of pandemic H1N1 isolates in mice, we produced mouse-adapted variants of A(H1N1)pdm09 strain by serial lung-to- lung passages in BALB/c mice. After total of 7 passages we got the lethal strains to BALB/c mice (BALB/c-MA) with meaning of 50% lethal dose 1,2 lgTCID50/ml. Hematoxylin-eosin staining, immunohistochemistry for type A influenza nucleoprotein antigen, and real-time reverse transcription-PCR assay for viral RNA were performed. Complete genome sequences of the wild-type and mouse-adapted A (H1N1)pdm09 influenza viruses revealed 19 amino acid substitutions in different viral proteins (HA, NA, NS2, NS1, PB2, PB1, NP). In lung tissue under the influence of not adapted and mouse-adapted variants of A(H1N1)pdm09 influenza viruses developed interstitial pneumonitis, but it is noted the greatest degree of inflammation in case of infection of the strain BALB/c-MA. Comparative analysis revealed accumulation of viral titers in the brain (3,75±0,22 lgTCID50/ml), liver (2,5±0,5 lgTCID50/ml) and the kidney (0,74±0,48 lgTCID50/ml) in case of infection only of the strain BALB/c-MA. Immunohistochemistry staining of viral antigens was demonstrated in the lung pneumocytes and mucous glands under influence of both wild-type and mouse-adapted viruses. But only in case of infection with BALB/c-MA immunostaining was detected also in the brain, liver, kidney and in the intestine. This study demonstrates cellular localization of positive-stranded A(H1N1)pdm09 RNA in the lungs, brain, liver, kidney and in the intestine that suggests viral replication of the mouse adapted variants of A(H1N1)pdm09 influenza virus in these tissues. The study was supported by a grant from the Russian Scientific Foundation (project No.17-44-07001).

Recent Publications

1. Prokopyeva EA, Sobolev IA, Prokopyev MV, Shestopalov AM (2016). Adaptation of influenza A(H1N1)pdm09 virus in experimental mouse models. Infect Genet Evol. 2016 Apr;39:265-271. doi: 10.1016/j.meegid.2016.01.022.
2. Prokopyeva EA, Romanovskaya AA, Sharshov KA, Zaykovskaya AV, Alekseev AY, Shestopalov AM (2017) Pathogenicity assessment of wild-type and mouse-adapted influenza A(H1N1) pdm09 viruses in comparison with highly pathogenic influenza A(H5N1) virus. Histol Histopathol. 2017 Oct;32(10):1057-1063. doi: 10.14670/HH-11-866.
3. Yarushkin AA, Kazantseva YA, Prokopyeva EA, Markova DN, Pustylnyak YA, Pustylnyak VO. (2016) Constitutive androstane receptor activation evokes the expression of glycolytic genes. Biochem Biophys Res Commun. 2016 Sep 23;478(3):1099-105. doi: 10.1016/j.bbrc.2016.08.075.

Biography

Prokopyeva Elena has completed her PhD at the age of 29 years from FBRI State Research Center of Virology and Biotechnology 'Vector'(Koltsovo, Russia). Dissertation title: «Phenotypic and genotypic properties of pandemic influenza A(H1N1)pdm09 virus during adaptation to mice of different genotypes». She conduct postdoctoral studies from Novosibirsk State University and Research Center of Experimental and Clinical Medicine (Novosibirsk, Russia). She is the researcher of the Laboratory experimental simulation and pathogenesis of infectious diseases, and the teacher of the course "Embryology" and " General Histology" at Novosibirsk State University (NSU). She has published more than 25 papers in reputed journals. She has been conducting supervision of undergraduates at NSU since 2016. Also Prokopyeva Elena has obtained different honors and awards in the field of Virology, Pathology and Medical Microbiology.

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