

## Whole-genome characterization of influenza A viruses circulated in Russian Federation in 2015-2018 epidemic seasons

### Content

**BACKGROUND:** Implementation of NGS technology in the framework of influenza surveillance in Russia significantly improved identification of possible factors that could influence the course of epidemics and the impact of internal genes evolution on pathogenicity and transmission of influenza viruses. Whole-genome sequencing of influenza A viruses selected by the epidemic periods and geography spread (30 regions) was performed.

**METHODS:** rRT-PCR, whole-genome amplification, Illumina sequencing, phylogenetic analysis.

**RESULTS:** All analyzed influenza A(H1N1)pdm09 viruses belonged to phylogenetic group 6B.1 and demonstrated the slow antigenic drift. A set of mutations was revealed in internal genes of Russian A(H1N1)pdm09 viruses leading to amino acid substitutions: D2E and E125D (transport of host mRNA) in NS1 protein; M83I (nuclear transport signal site) in NEP protein; M105T in NP protein; Q208K in M1 protein; N204S in PA-X protein (possible virus-host interactions). The incidence rate of these substitutions increased from about 10% in 2014-2015 to 85% in 2015-2016 and up to 100% in 2017-2018.

A(H3N2) sequenced viruses consistently clustered in two groups corresponding to 3C.2a and 3C.2a1 on all trees, with several intra-group reassortant exceptions (HA and PA genes).

Some A(H3N2) viruses had 11 and 25 aa truncated PB1-F2 protein, belonged to subgroup 3C2a.1, possessed I58V substitution in HA1 and clustered together on phylogenetic trees for all genome segments. PB1-F2 truncation is seldom observed in A(H3N2) viruses (the incidence rate less than 1% during the last decade). The functional significance of this change may be related to the virulent properties of the virus or its transmission ability.

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