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Genetic diversity of human metapneumovirus (Pneumoviridae: *Metapneumovirus*) in Russia: results of molecular analysis

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Abstract

Introduction. Human metapneumovirus (hMPV) holds significant epidemiological importance, being a dominant cause of lower respiratory tract infections in children under two years of age and individuals over 65. Multiple infections with hMPV throughout a person's life are possible due to the antigenic and genetic variability of the virus. However, the genetic variability of hMPV circulating in Russia remains unexplored.

Aim of the study. The aim of this study was to test a protocol for whole-genome sequencing of hMPV to assess the genetic diversity of metapneumoviruses circulating in certain regions of Russia.

Materials and methods. Nasopharyngeal swabs were collected from patients of different ages with acute respiratory viral infections (ARVI) tested positive for hMPV using polymerase chain reaction (PCR). From some of the samples, viral isolates were obtained in cell culture. Whole-genome sequencing was performed on both swabs and isolates using the MiSeq Illumina platform, followed by phylogenetic analysis.

Results. For the first time in Russia, whole-genome sequencing of 44 hMPV strains circulating from 2017 to 2024 was conducted. Their genetic group affiliation was described, with the A2b2 clade shown to dominate. It was confirmed that the greatest variability among genes encoding viral surface proteins was observed in the G gene, while changes in the F gene were minimal during the studied period.

Conclusion. The study provides insights into the genetic diversity of hMPV strains circulating in various regions of the Russian Federation. Understanding the genetic variability of hMPV is crucial for comprehending viral evolution, transmission dynamics, and mechanisms of immune evasion, which influence the development of vaccines and antiviral drugs.

Keywords: *human metapneumovirus; whole-genome sequencing; genetic variability; gene F; gene G; duplications*

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ОРИГИНАЛЬНОЕ ИССЛЕДОВАНИЕ
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Генетическое разнообразие метапневмовируса человека (Pneumoviridae: *Metapneumovirus*) в России: результаты молекулярного анализа

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Резюме

Актуальность. Метапневмовирус человека (*Human metapneumovirus*, hMPV) имеет большое эпидемиологическое значение, являясь доминирующей причиной инфекций нижних дыхательных путей у детей младше 2 лет и лиц старше 65 лет. Возможно многократное инфицирование hMPV в течение жизни человека ввиду антигенной и генетической изменчивости возбудителя. При этом генетическая изменчивость hMPV, циркулирующих в России, остается неизученной.

Цель работы. Апробация протокола полногеномного секвенирования hMPV для оценки генетического разнообразия метапневмовирусов, циркулирующих в отдельных субъектах России.

Материалы и методы. Исследовали назофарингеальные мазки от пациентов разного возраста с острыми респираторными вирусными инфекциями, положительные в полимеразной цепной реакции на hMPV. Из части образцов вирус выделяли на клеточной культуре. На платформе Illumina MiSeq проведено полногеномное секвенирование вирусов hMPV из мазков и изолятов с последующим филогенетическим анализом.

Результаты. Впервые в России проведено полногеномное секвенирование 44 hMPV, циркулировавших в период с 2017 по 2024 г., описана их принадлежность к генетическим группам, показано доминирование клайда A2b2. Подтверждено, что наибольшее разнообразие в генах, кодирующих поверхностные белки вируса, отмечено для гена *G*, в то время как в гене *F* в изучаемый период изменения были минимальны.

Заключение. Проведенное исследование дает представление о генетическом разнообразии вирусов hMPV, циркулирующих в отдельных субъектах Российской Федерации. Изучение генетической изменчивости hMPV имеет решающее значение для понимания вирусной эволюции, динамики передачи и механизмов иммунного ускользания, которые влияют на разработку вакцин и противовирусных препаратов.

Ключевые слова: *метапневмовирус человека; полногеномное секвенирование; генетическая изменчивость; ген F; ген G; дупликации*

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Introduction

Human metapneumovirus (Orthornavirae: Pneumoviridae: *Metapneumovirus*: *Metapneumovirus hominis* (ICTV 2024), hMPV) was first identified in the Netherlands in 2001 [1]. The genome of the virus is represented by single-stranded RNA with negative polarity. The closest relative of human metapneumovirus is human respiratory syncytial virus (*Orthopneumovirus hominis*, hRSV), which also belongs to the Pneumoviridae family [2]. Both viruses share a number of common characteristics, such as genome structure and transmission routes, but differ in specific features of interaction with host cells and pathogenetic mechanisms. The study of evolutionary relationships and genetic features of hMPV is important for understanding the mechanisms of pathogenicity and developing effective methods of prevention and treatment.

The hMPV genome, which is about 13,000 nucleotides long, consists of 8 genes encoding 9 proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion

protein (F), matrix proteins 2 (M2-1 and M2-2), small hydrophobic (SH) protein, glycoprotein (G), and large (L) polymerase protein [3, 4]. Among them, two surface glycoproteins, fusion protein (F) and attachment protein (G), play a key role [4, 5]. These molecules allow virus entry into host cells and promote evasion of the immune response [6]. G protein mediates virus attachment to the cell surface and F protein is responsible for membrane fusion processes, making these proteins important targets for the study and development of therapeutic approaches [7]. The virus has tropism to airway epithelial cells, where it induces pronounced cytopathic effects [8]. One of the most characteristic manifestations of the pathomorphologic process is the formation of giant multinucleated epithelial cells – syncytium, which promotes the spread of the virus in tissues and enhances its pathogenicity [9].

Human metapneumovirus is classified into two major genetic lineages, A and B, which are further subdivided into the corresponding sublineages A1, A2, B1 and B2 [10, 11], given the genetic diversity of the virus [12]. Repeated infection with hMPV is associated with antigenic variability of the virus surface proteins, which makes it difficult to form persistent immunity [12, 13]. The most genetically close pneumovirus to hMPV is avian metapneumovirus type C. According to calculations, the closest common ancestor of these viruses could have existed 215–268 years ago [14, 15]. Currently, cases of zoonotic transmission of metapneumoviruses are unknown, and experiments on infection of birds with hMPV have not resulted in productive infection [16]. Presumably, the separation of human metapneumovirus types may have occurred less than 100 years ago [14].

There was no systematic surveillance of this virus in most countries, and for a long time the molecular epidemiology of hMPV remained poorly understood [6, 17]. However, in recent years, due to the increased interest in the study of respiratory syncytial virus, the number of studies on metapneumovirus has also increased[1]. In the context of globalization and increasing population mobility, antigenic and molecular characterization of modern hMPV isolates has become critical for understanding its global distribution and evolutionary dynamics [11, 13].

From an epidemiologic point of view, hMPV is one of the leading causes of acute respiratory infections of non-influenza etiology worldwide [9, 18]. It primarily affects newborns and children under 2 years of age, people over 65 years of age, and immunocompromised patients, with seasonal peaks usually occurring in late winter and spring [10, 19]. Transmission of the pathogen occurs predominantly by airborne droplet transmission, with contact and household contact possible, and the incubation period is estimated to be 4–6 days [4, 12, 20–22]. Clinical manifestations range from mild upper respiratory tract symptoms to severe lower respiratory tract infection, including bronchiolitis and pneumonia [23, 24]. Epidemiologic studies show that seroprevalence in the population exceeds 90% after the age of 5 years, suggesting almost universal early infection (as for hRSV) [25].

Currently, the mass media are actively discussing the increase in the incidence of metapneumovirus infection in the northern provinces of the People's Republic of China and in a number of other countries[1]. At the same time, given the pronounced seasonality of circulation, it should be noted that the increase in the number of metapneumovirus infection cases is natural for this time of year [4, 12, 20]. According to official information posted on the website of the World Health Organization, «according to the latest acute respiratory infection surveillance data provided by the Center for Disease Control and Prevention of China as of December 29, 2024, there is an upward trend in the prevalence of acute respiratory infections, including those caused by seasonal influenza viruses, RSV and hMPV, as expected for this time of year (winter) in the Northern Hemisphere»[1].

Despite the fact that hMPV has been known for more than 20 years, its genetic diversity has not been sufficiently characterized both in the world and in Russia [1, 4, 24]. In addition, despite the important role of pneumoviruses in the etiologic structure of respiratory infections, information on the prevalence of hMPV in different regions is sketchy, and the nature of its circulation is practically unstudied [19, 26]. Thus, the study of the patterns of evolution of pneumoviruses, in particular hMPV, is necessary and relevant, given the continuing burden of pneumovirus infections, especially among children of younger age groups.

The aim of the study was to investigate the genetic diversity of human metapneumoviruses identified in Russia by analyzing the genetic variations of fusion (F) and attachment (G) proteins.

Materials and methods

Clinical samples. The study included nasopharyngeal swab samples from hospitalized patients with respiratory symptoms collected between 2016 and 2024, mainly in St. Petersburg and the Leningrad Region as part of hospital surveillance for acute respiratory viral infections (ARVI). Total RNA extraction was performed using the NAmagP 2000 RNA extraction kit (Biolabmix LLC, Russia). Metapneumovirus RNA detection in clinical material was performed using the AmpliSens ARVI-screen-FL reagent kit (Central Research Institute of Epidemiology of Rospotrebnadzor, Russia) by real-time reverse transcription polymerase chain reaction (PCR) method.

Cell lines. The cell line LLC-MK2 (*Macaca mulatta* monkey kidney) obtained from ATCC (American Type Culture Collection, USA) was used for hMPV isolation. The cell monolayer was cultured using DMEM nutrient medium (LLC Biolot, Russia) supplemented with 10% fetal bovine serum (LLC Biolot, Russia), 1% mixture of penicillin G and streptomycin antibiotics (50,000 units/vial and 50 g/vial, respectively) (LLC Biolot, Russia). Cell culture transfer was performed on the 7th day. Seeding concentration was $2.5–5.0 \times 10^5$ cells/mL. Cells were grown at 37 °C in an incubator with 5% CO_2.

[1]World Health Organization: Disease Outbreak News; Trends of acute respiratory infection, including human metapneumovirus, in the Northern Hemisphere 2025 [7 January 2025]. Available at https://www.who.int/emergencies/disease-outbreak-news/item/2025-DON550

Media. **Support medium for virological experiments on LLC-MK2 cell culture.** Per 100 mL of DMEM medium, 2.6 mL of serum albumin V fraction (Sigma, Germany), 1.6 mL of HEPES buffer (Sigma, Germany), 100 µL of gentamicin solution for cell cultures (Biolot LLC, Russia), 100 µL of TPCK-trypsin solution (2 µg/mL) (Sigma, Germany) were added. **Cell washing medium.** 100 µL of gentamicin solution for cell cultures, 100 µL of TPCK-trypsin solution (2 µg/mL) were added per 100 mL of DMEM medium.

Cultivation of metapneumovirus. The daily monolayer of LLC-MK2 cells in special plastic tubes with beveled bottom (Nunc, Denmark) was washed twice with 2 mL cell washing medium. PCR-positive materials from patients were added 0.2 mL each into 2 vials with cell culture and after incubation for 40–60 min at 36 °C, 1.8 mL of maintenance medium was added. After that, the vials were incubated at 36 °C, monitoring the monolayer condition daily in an inverted microscope. In the absence of pronounced cytopathic effect (CPE), the samples were incubated at 36 °C for up to 14 days. In the absence of CPE on the 14th day, cells were destroyed by freezing/thawing, pooled pools of culture fluid were prepared (from 2 vials from each sample) and the following passaging was performed in 2 vials with a daily monolayer of LLC-MK2 cells with registration of reproduction by CPE. Three consecutive passages were performed for each sample. In the presence of initial or pronounced CPE, the presence of virus was further confirmed using a PCR test system with real-time detection of results. The primer sets and reaction conditions are described in a study by S. Sugimoto et al. [27].

Whole genome amplification was performed according to the protocol of K. Groen et al. [28] with modifications. Sequencing of the full-length hMPV genome was performed using the DNA Prep reagent kit from Illumina (USA). The complementary DNA was purified on magnetic particles. Genomic libraries were sequenced on the MiSeq Illumina platform using MiSeq Reagent Kit v3 600-cycle. The BWA algorithm was used to align the resulting reads to a reference sequence. Samtools and Ivar software were used to obtain consensus sequences.

Comparative phylogenetic analysis of nucleotide sequences was performed by the maximum likelihood method using the RAxML algorithm and the GTRGAMMA nucleotide substitution model. Statistical support of tree branches was determined by the rapid bootstrap method with 1000 replications. The phylogenetic tree was midpoint rooting. Ancestral sequences were reconstructed using the PAML algorithm in Treesub[2]. Phylogenetic trees were visualized and annotated using Figtree and Inkscape software [28]. The ggtree library in R was used to visualize the whole-genome phylogenetic tree. The global dataset of complete human metapneumovirus genomes available on the Nextstrain platform (https://nextstrain.org/hmpv) – 682 genomes deposited in the GenBank database – was used for analysis. The dataset was filtered using the Nextclade tool [31]. The number of unsequenced positions (totalMissing < 1500) and the quality indicator for the presence of unique mutations (qc.privateMutations.status not equal to «bad») were used as criteria. Phylogenetic signal in hMPV whole-genome sequences was determined using the TempEst program. The external domain of hMPV G protein was analyzed using the Chi-Score application.

Ethical approval. The study was conducted with voluntary informed consent of patients. The study protocol was approved by the Ethical Committee of the A.A. Smorodintsev Research Institute of Influenza (protocols No. 215 of 31.01.2024, No. 194 of 12.12.2022, No. 178 of 10.01.2022, No. 161 of 14.12.2020, No. 149 of 18.12.2019, No. 136 of 21.12.2018, No. 3120 of 18.12.2017).

Results

According to PCR diagnostic data, during the epidemic seasons 2016–2024, the circulation of metapneumovirus in St. Petersburg and the Leningrad Region was unstable and low, averaging 9.7% of all cases positive for viral pathogens, excluding influenza and COVID-19 pathogens (**Fig. 1**). The proportion of positive metapneumovirus cases was relatively high only in the 2020–2021 season at 21.4%. In the following season 2021–2022, the contribution of hMPV was minimal (2.5%); in comparison, the proportion of laboratory-confirmed rhinovirus infection in this season was 49.2%.

Sequencing resulted in 44 whole-genome sequences of metapneumoviruses isolated from patients from St. Petersburg and Leningrad Region (43) and Yamalo-Nenets Autonomous District (1) during 4 epidemic seasons of 2018–2024. Of these, 11 circulated before the pandemic (epidemic seasons 2017–2018 and 2018–2019), and 33 circulated during the epidemic seasons 2022–2023 and 2023–2024. Despite the high proportion of hMPV in circulation in the 2020–2021 season, whole-genome sequences of the virus could not be obtained from primary samples. Virus isolation was also unsuccessful, which may be due to the sampling medium at the peak of the pandemic being unsuitable for said process. According to phylogenetic analysis, the majority of sequenced metapneumoviruses belonged to the A2b2 genetic clade (40 of 44), 1 virus was identified as belonging to the A2b1 clade, and 3 to the B2 clade (**Fig. 2**, **Table 1**). According to the results of the global dataset analysis, the proportion of the A2b2 clade ranged from 27 to 100% in different years.

The hMPV viruses of genetic lineage A2b2 from individual subjects of Russia formed three phylogenetic clusters close to the viruses from Switzerland, the USA, and Australia 2021–2024 according to the data of whole genome analysis. It is interesting to note that each of the clusters included viruses collected in different epidemic seasons. This may be explained by a weak temporal signal [30] or by the low rate of evolution of this pathogen in combination with global spread and numerous transfers of the virus from one geographic region to another and back. The TempEst program was used to check the level of temporal signal in whole genome sequences of hMPV.

[2]Treesub: annotating ancestral substitutions on a tree [1 February 2025]. Available at: https://github.com/tamuri/treesub.

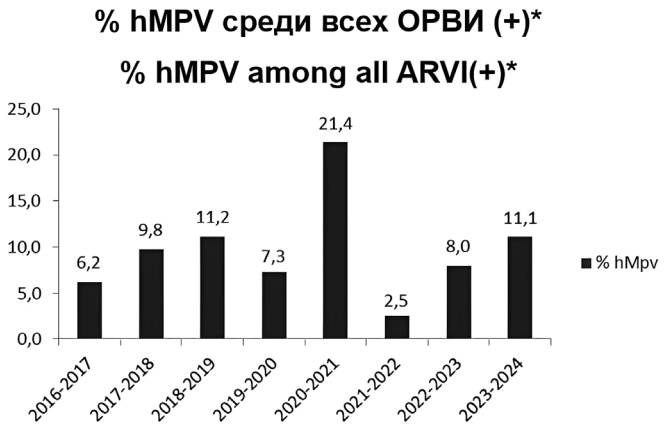

Fig. 1. The percentage of samples positive for metapneumovirus in the structure of acute respiratory viral infections by seasons 2016–2024.

* – samples are positive only for respiratory viruses (rhino-, adeno-, boca-, metapneumo-, coronavirus, parainfluenza viruses and human respiratory syncytial virus) excluding influenza viruses and SARS-CoV-2.

Рис. 1. Доля положительных на метапневмовирус образцов в структуре ОРВИ по сезонам 2016–2024 гг.

* – образцы положительны только на респираторные вирусы (рино-, адено-, бока-, метапневмо-, коронавирусы, вирусы парагриппа и респираторно-синцитиальный вирус человека) исключая вирусы гриппа и SARS-CoV-2.

Table 1. Genetic lineages of human metapneumoviruses in the epidemic seasons of 2017–2024

Таблица 1. Принадлежность метапневмовирусов человека к генетическим линиям в эпидемические сезоны 2017–2024 гг.

Epidemic season Эпидемический сезон	Total Всего	A2b1	A2b2	B2
2017–2018	8	0	6	2
2018–2019	3	0	3	0
2022–2023	10	0	10	0
2023–2024	23	1	21	1

The analysis demonstrated a significant correlation ($r > 0.9$, $R^2 > 0.8$) between genetic distance and sample collection time, indicating the presence of temporal signaling in hMPV data from different subtypes (**Fig. 3**). Thus, the clustering of the 2018–2024 hMPV genomes may indicate that sufficient evolutionary changes do not occur in the genome over a period of 5–6 years to reliably differentiate viruses of different epidemic seasons. However, at longer time intervals such differentiation becomes possible (Fig. 2), which can be seen from the way viruses of different years are grouped on the color scale.

The results of the analysis of the *F* and *G* genes show minimal genetic changes in the *F* gene and significant genetic variability in the G glycoprotein (**Figs. 4–7**). Metapneumoviruses of the A2b2 clade collected in 2017–2024, with the exception of two viruses, form a single group on the phylogenetic tree (Fig. 4). Interestingly, the A2b2 genetic lineage has no characteristic distinctive amino acid substitutions in F.

Most of the detected amino acid polymorphisms were localized in the F1 subunit of the F fusion protein. No amino acid substitutions leading to a change in the N-glycosylation profile were detected in the F protein of both hMPV subtypes (Figs. 4, 6).

The *G* gene is highly covariable and encodes a mucin-like glycoprotein of disordered structure with a large number of potential O-glycosylation sites. The coding sequence of the *G* gene can be divided into intravirion (1–30 aa), transmembrane (31–51 aa), and outer domains. The intravirion and transmembrane domains of hMPV of different subtypes have a high degree of similarity: 36 amino acid residues (a.a.r.) out of 51 (more than 70%) are conserved in 99–100% of viruses of subtypes A2 and B2. For the external domain, this figure drops to a noisy level (less than 30%). It is interesting to note that hMPV subtype A2 is characterized by the occurrence of extended duplications: thus, in the *G* gene of 36 out of 37 metapneumoviruses of subtype A2 from all three regions of Russia, a region with a 111-nucleotide-long duplication was detected. In the *G* gene of subtype B2, extended duplications were not detected.

It has been shown that disordered regions of proteins can have non-random organization and can be divided into modules using the χ^2 homogeneity test [31]. Using the Chi-Score tool, we analyzed the external domain of protein G of hMPV subtypes A2 and B2 (**Fig. 8**).

It was shown that the outer domain of the G protein hMPV subtype A2 can be divided into two modules – module 1 (52–139 a.a.r.) and module 2 (140 a.a.r. – C-terminus of the protein), with module 2 characterized by extended duplications (up to 37 a.a.r. in length). The repeats consist of *S1*, *L1*, *S2*, *L2* sites separated by conserved RTSSA spacer sequences (**Fig. 9**). It should be noted that the repeat sites are not 100% homologous and may contain substitutions at different positions.

About 57% of the subtype A2 metapneumoviruses analyzed contained only *S1* and *L2* regions (including 1 virus of A2b1 lineage (hMPV/Russia/SPE-RII-7947S/2023), 41% additionally contained the L1 region (including 36 Russian A2b2 lineage viruses), and only less than 2% of the viruses contained all repeats (**Table 2**).

The external domain of the G protein hMPV subtype B2 can be divided into four modules – module 1, modules 2 and 4, which are mucin-like domains, and module 3 between them, which is a Glu-Lys-rich spacer of 14–18 a.a.r.

Discussion

Human metapneumovirus is one of the respiratory pathogens that have a significant impact on health, primarily in children and the elderly. The study revealed important aspects of hMPV circulation and genetic variability in three regions of the Russian Federation, which contributes to understanding the dynamics of viral evolution.

One of the key results of the work was the establishment of the dominance of the A2b2 genetic clade in Russian hMPV isolates in the period from 2017 to 2024.

The phylogenetic analysis showed a high degree of similarity between Russian hMPV isolates and isolates

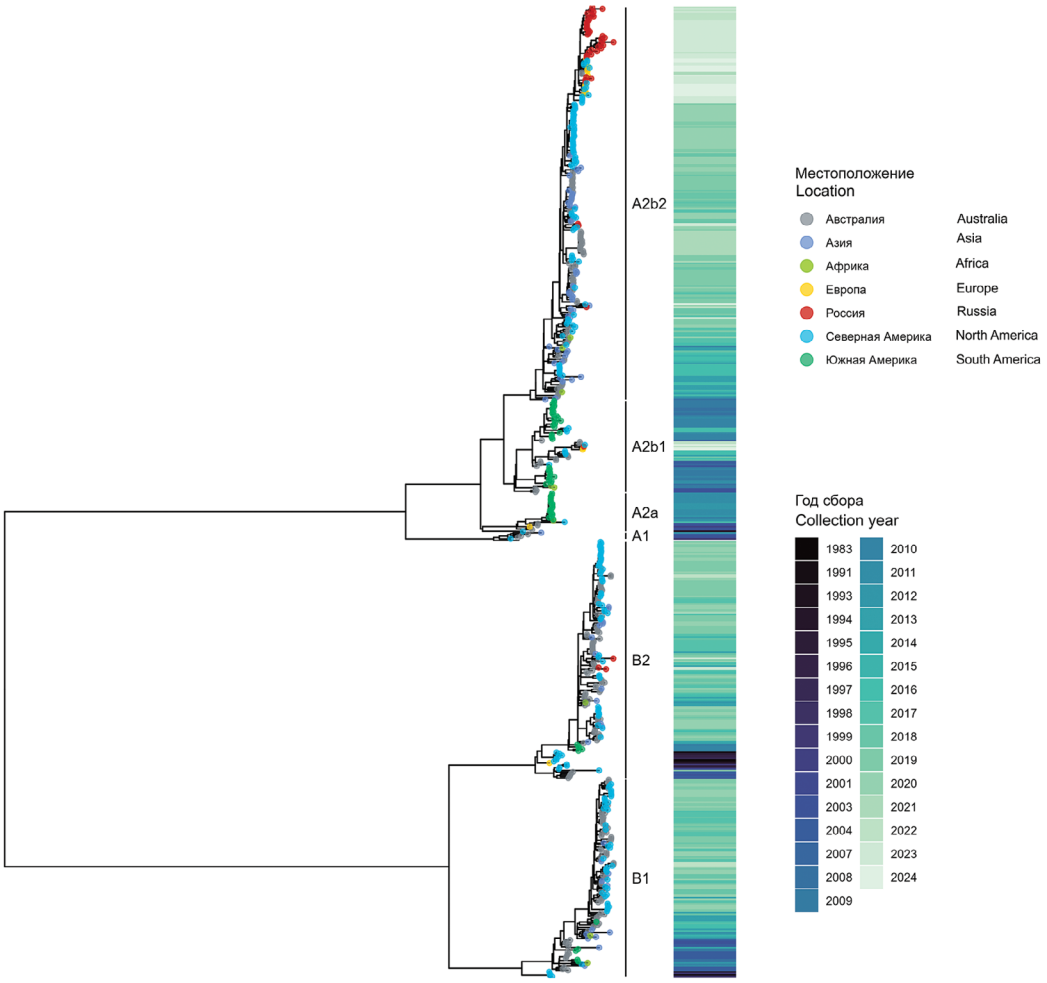

Fig. 2. Global diversity of human metapneumoviruses based on whole-genome sequencing data.
Isolates from the Russian Federation are marked in red.

Рис. 2. Глобальное разнообразие метапневмовирусов человека по данным полногеномного секвенирования.
Красным отмечены изоляты из Российской Федерации.

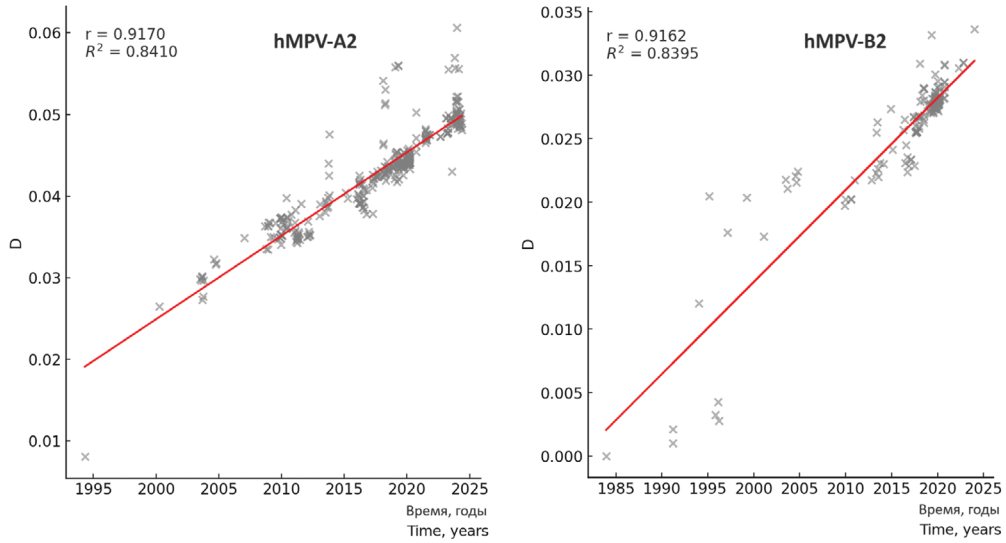

Fig. 3. Temporal signal in whole genome sequences of hMPV.
Subtype A2 (left), subtype B2 (right). D – genetic distance of root-to-tip divergence.

Рис. 3. Определение временно́го сигнала в полногеномных последовательностях hMPV.
Субтип A2 (слева), субтип B2 (справа). D – генетическая дистанция от корня до листьев филогенетического дерева (root-to-tip divergence).

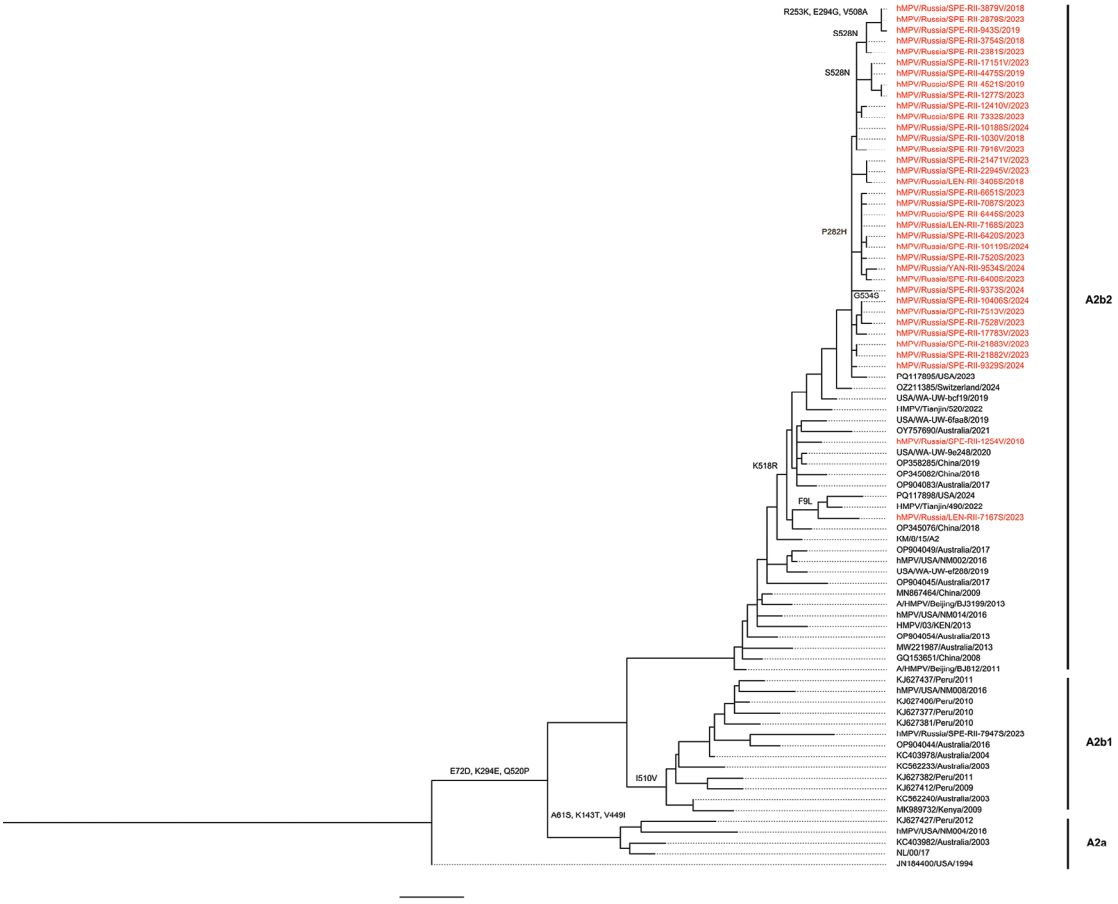

Fig. 4. *F* gene phylogenetic tree of subtype A2 human metapneumovirus.

Viruses identified in three regions of the Russian Federation are marked in red.

Рис. 4. Филогенетическое дерево по гену *F* метапневмовируса человека подтипа A2.

Красным цветом отмечены вирусы, выявленные в трех регионах Российской Федерации.

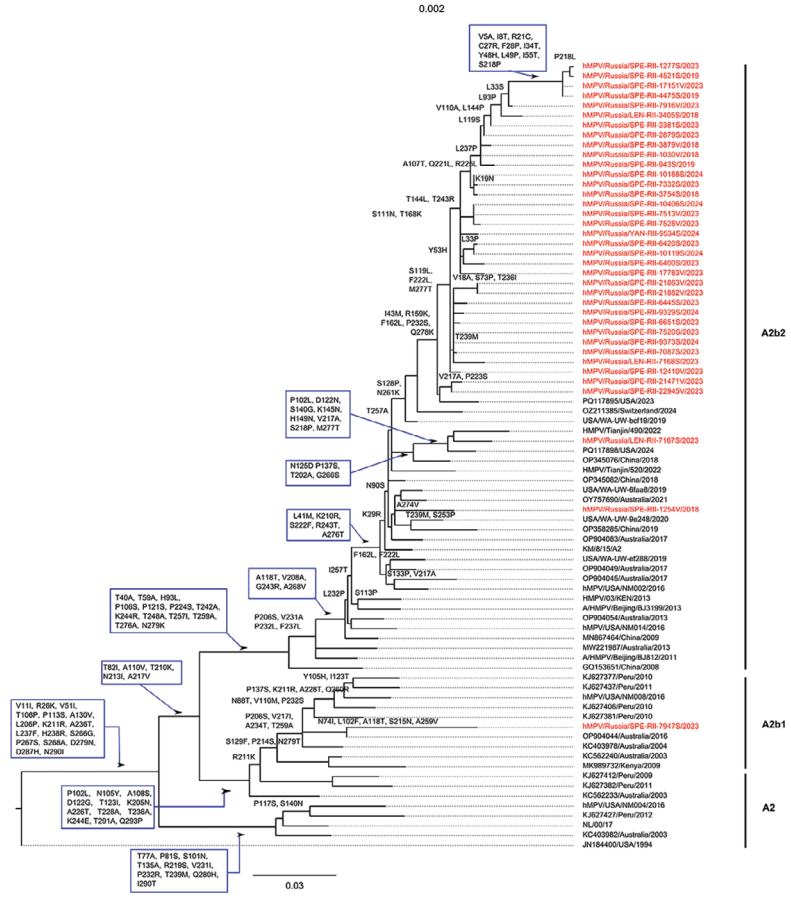

Fig. 5. *G* gene phylogenetic tree of subtype A2 human metapneumovirus.

Viruses identified in three regions of the Russian Federation are marked in red.

Рис. 5. Филогенетическое дерево по гену *G* метапневмовируса человека подтипа A2.

Красным цветом отмечены вирусы, выявленные в трех регионах Российской Федерации.

Fig. 6. *F* gene phylogenetic tree of subtype B2 human metapneumovirus.

Viruses identified in Saint Petersburg are marked in red.

Рис. 6. Филогенетическое дерево по гену *F* метапневмовируса человека подтипа B2.

Красным цветом отмечены вирусы, выявленные в Санкт-Петербурге.

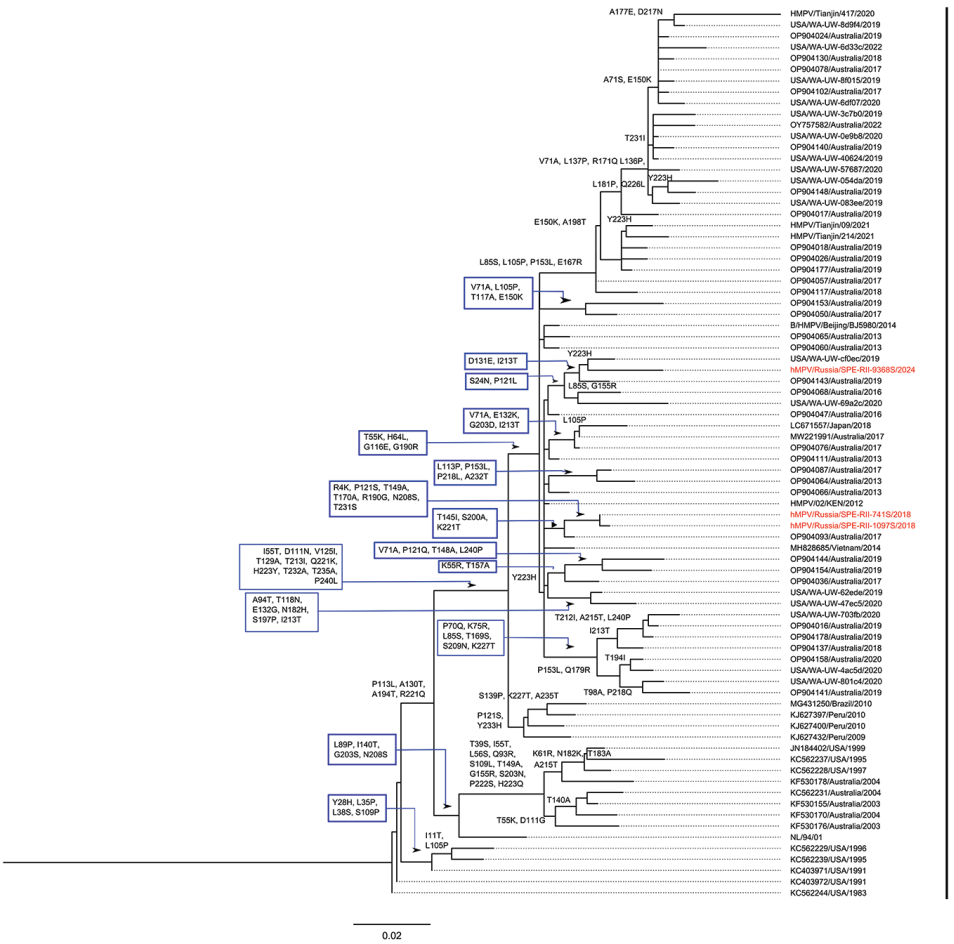

Fig. 7. G gene phylogenetic tree of subtype B2 human metapneumovirus.

Viruses identified in Saint Petersburg are marked in red.

Рис. 7. Филогенетическое дерево по гену *G* метапневмовируса человека подтипа B2.

Красным цветом отмечены вирусы, выявленные в Санкт-Петербурге.

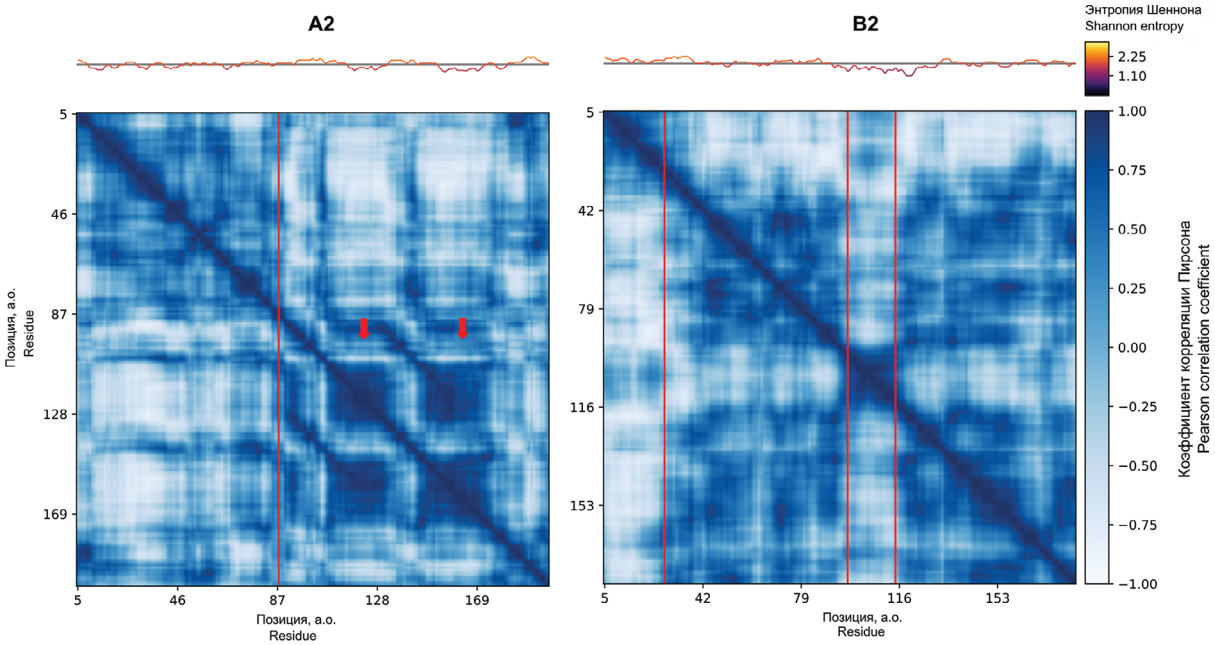

Fig. 8. Heat map of G protein external domains of hMPV subtypes A2 (left) and B2 (right) based on Chi-Score data (Brendan S, et al., 2023 [31]).
Red arrows indicate regions of extended duplications.

Рис. 8. Тепловая карта внешних доменов белка G вирусов hMPV подтипов A2 (слева) и B2 (справа) по данным инструмента Chi-Score (Brendan S. и соавт., 2023 [31]).
Красными стрелками отмечены участки протяженных дупликаций.

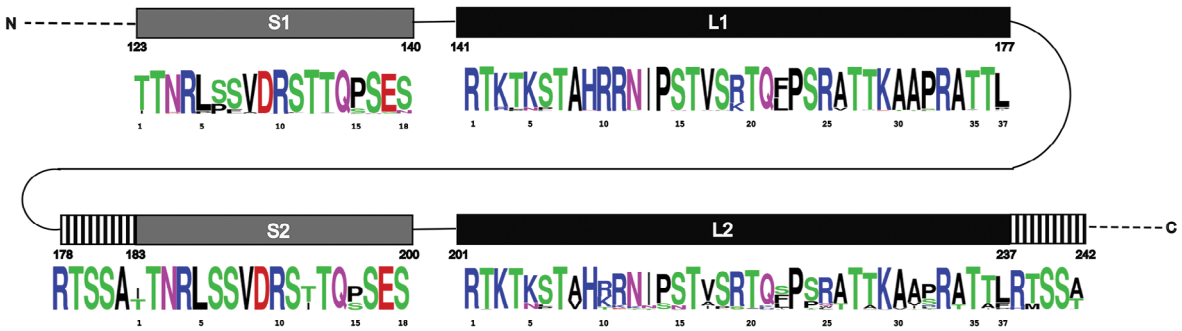

Fig. 9. Structure of the duplication sequences in the G protein external domain of the hMPV subtype A2.

Рис. 9. Структура последовательности с повторами внешнего домена белка G hMPV подтипа A2.

Table 2. Different combinations of duplications in the G protein external domain of the studied hMPV subtype A2

Таблица 2. Различные комбинации повторов последовательностей внешнего домена белка G подтипа A2 у исследованных вирусов hMPV

Duplications Наличие повторов				Number of isolates containing this combination/ Number of sequenced isolates Количество изолятов, содержащих данную комбинацию/N секвенированных	Note Примечание
S1	*L1*	*S2*	L2	6/338	No isolates from Russia Нет российских изолятов
S1	*L1*	–	*L2*	140/338	36 subtype A2b2 isolates from Russia 36 российских изолятов линии A2b2
S1	–	–	*L2*	192/338	1 subtype A2b1 isolate from Russia 1 российский изолят линии A2b1

circulating in Europe and Asia, which emphasizes the importance of cross-border epidemiological monitoring.

Comparison of the results of phylogenetic analysis of complete genomes and surface antigen coding sequences shows the same clade separation for all the studied viruses, which suggests a low probability of recombination between different hMPV strains.

Duplications of 54 and 111 nucleotides were detected in the *G* gene of 84% of Russian isolates belonging to the A2b lineage A study by P. Parida et al. detected

a 180-nucleotide duplication in the *G* gene of hMPV A2c lineage [32]. Similar results were obtained in earlier studies in Spain between 2014 and 2016 [33], in Croatia between 2014 and 2017 [34] and in Japan in 2014 [35]. Also in the same time period, more than 50% of hMPV isolates had 111 nucleotide duplications (Japan, 2014–2016 [36], Croatia, 2014–2016 [34], China, 2017. [37]). In a study conducted by M. Pinana et al. in Spain, it was hypothesized that A2c sublineage may replace A2a and A2b sublineages, and A2c strains with duplications may soon replace wild type A2c due to a better mechanism to evade the immune response resulting from duplications [33]. The presence of duplications in the *G* gene in most Russian isolates indicates the possible formation of new antigenic variants that may be of epidemiologic significance. These changes require further study, as they could potentially affect the efficacy of vaccines.

Conclusion

The molecular structure of human metapneumovirus circulating in 2017–2024 in selected subjects of Russia was studied in this work, which allowed us to obtain unique data on its genetic diversity. The results of the study emphasize the significance of an integrated approach to the study of the virus, including monitoring of circulation, determination of genetic variability and assessment of virus evolution. This study lays the foundation for further analysis of hMPV evolutionary processes and assessment of its impact on public health, which is of practical and scientific importance for the improvement of molecular diagnostic methods, risk assessment of the spread of new genotypes, epidemiological monitoring, control strategies for acute respiratory infections and vaccine development.

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