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DOUBLE-STRANDED DNA VIROME OF THE SMALL ARAL SEA

Abstract. The study of environmental biodiversity is the most important direction of research in biological disciplines. Particularly relevant is the study of degrading ecosystems, because this may indicate the direction in restoring the equilibrium in the ecosystem. The taxonomic diversity of double-stranded DNA (dsDNA) virome in the Small Aral Sea is dealt with the article. The choice of the research object is primarily due to the fact that dsDNA virome is the most numerous component of any ecosystem. Virome of the research sample was studied by multiple parallel sequencing method. As a result of the sequencing data processing, 43009 viral sequences were obtained. A comparative study of viral sequences showed that most viruses possess with dsDNA genome. It was found that among dsDNA virome both autochthonous and allochthonous viruses are present. The most numerous were autochthonous viruses that infect organisms of three evolutionary domains and belong to the *Caudovirales* order and nucleocytoplasmic viruses of the *Iridoviridae, Mimiviridae* and *Phycodnaviridae* families. Despite the small number (3%), among the allochthonous viruses, strains of 13 different families that can cause infections in humans and animals were detected, which indicates an anthropogenic impact on the Aral Sea. Studies show a large genotypic diversity of the Aral Sea viruses, and emphasize the need for more comprehensive analysis of those viruses that occur in one of the world's largest saline water ecosystems.

Key words: the Aral Sea, virome, bacteriophages.

Introduction. For the first time, aquatic viruses were recognized as pathogens of fish diseases such as pancreatic infection, necrosis and Oregon sockeye disease in the early 60s of the 20th century [1]. Since then, it has been proven that viruses affect absolutely all representatives of marine life from bacteria to protozoa, mollusks, crustaceans, fish and mammals [2]. Since the early 1990s, aquatic viruses have begun to be perceived not only as plant and animal pathogens, but also as one of the key factors in regulating interspecific interactions in ecosystems and the circulation of nutrients.

Viruses have a significant impact on the species and numerical composition of the main producers and decomposers of pyramid of numbers. Since Karl-Heinz Moebus' pioneering work on bacteriophages isolating from the waters of the North Atlantic [3, 4], research in marine viruses has developed into significant and independent direction of marine biology. Increasing interest in aquatic viruses is caused by an understanding of their key role in the balance and functioning of marine and freshwater ecosystems [5-7]. The invention of new methods and their technical improvement in detection and enumeration of marine viruses contributed to more detailed studies of their numbers and diversity [8]. It was found that viruses are the most abundant biological entities in the oceanic and marine environment [9]; reaching up to 10^8 viral particles in ml. Studies of aquatic viruses have become widespread, viruses of coral reefs [10], bottom sediments [11, 12], deep-sea biosphere [13], freshwater bodies [14] and others have been identified and studied. It has been proven that viruses are integrated inhabitants of all aquatic environments. Studies of recent decades confirm the key role of viruses in the regulation bacterial and algal mortality, in direction of their evolution, which in turn proves the indirect effect of viruses on both biogeocenosis and global biochemical cycles of oceans. The use of modern tools of molecular biology and next generation

sequencing in research of viruses and the genetic mechanisms of virus-host interaction has opened-up a huge amount of metagenomic data that showed a significant variety of aquatic viruses. Virome of aquatic ecosystems is considered the largest pool of unexplored genetic diversity on the globe, about 93% of the sequences not represented in the public databases [15]. Recently conducted metagenomic studies of 43 ocean sites identified 5,500 populations of only double-stranded DNA viruses [16]. Studies have shown that Flaviani et al found 254 unique viral phylotypes in a 250 ml sample of ocean water, even at very small scale, viral diversity can be significantly high, which confirms the difference between viruses in the world's oceans [17].

Of particular interest are studies of viral diversity in reservoirs with high salt content, one of which is the Aral Sea. In such environments, the distribution of viruses occurs along the gradient of salinity, and when the salinity level of the reservoir is above 20%, the level of the bacterial flora decreases rapidly. In this case, the number of heterotrophic nanoflagellates and infusorians decreases by approximately 25%, as a result the role of bacteriophages in the control of the number and species diversity of halophilic microbial communities increases frequently [18].

The aim of our research is to study the biodiversity of bacteriophages in the ecologically adverse region of the Aral Sea, which is the extreme salinity as soil and water. In our work, a metagenomic study of viral communities from the Bolshoi Saryshyganak Bay of the Small Aral Sea was conducted. The choice of location was due to a sharp increase the salinity of the region, which led to decrease the lake biodiversity. Critical morphological changes and progressive salinization have led to a profound change in the biological system of the sea. There has been a replacement of freshwater and brackish-water biological communities by broadly euryhaline species of marine and freshwater origin [19]. This makes it necessary to expand the research of the virome of the Small Aral Sea water basin, which is of interest from a theoretical and practical view.

Materials and methods. Virus containing water samples collecting. Water samples (10 liters) were collected into sterile containers. Samples were collected from surface of the Small Aral Sea at 1 week interval during the June 2018. The coordinates of the sampling point are 46 ° 37'22.6 "N 61 ° 28'25.6" E (figure 1).

Figure 1 – Place of the sampling point

Concentration of virus-containing samples. The seawater samples (300 L) were immediately filtered using a 300mm diameter cellulose membrane with a 3μm pore size and then filtered through a 0.22μm membrane, to remove the large organisms, such as zooplankton, phytoplankton, and bacteria. Next, the filtrate was concentrated to a volume of 500 ml using a tangential flow filtration (Vivaflow 200, Sartorius, with a total surface area 200 cm^2 of polyethersulfone membrane). To precipitate the virus particles, the concentrate was centrifuged using Beckman Coulter ultracentrifuge, Avanti J30I, at a speed of 29,000 rpm.

Isolation of nucleic acids. Nucleic acid was isolated from the obtained samples using the PureLinkViral DNA / RNA Mini extraction kit ("Invitrogen", USA) according to the manufacturer's protocol. A fluorescent dye specifically binding to a specific type of nucleic acid (double-stranded DNA, single-stranded DNA, RNA) was used to measure the concentration of nucleic acids. Quantitative measurements were performed using a Qubit dsDNA HS kit (High Sensitivity, Invitrogen, USA) according to the instructions for a Qubit 3.0 fluorimeter.

Virome libraries construction and sequencing. DNA libraries were designed using the Nextera XT DNA Sample Preparation Kit (llumina, USA) according to the manufacturer's protocol, which included the following steps: enzymatic DNA fragmentation, ligation of sequence adapters, pre-amplification of the library, selection of fractions of the desired length, clonal amplification of the selected library.

The amplified libraries were purifed with AMPure XP beads, the library's insert size was verified by Agilent 2100 Bioanalyzer and quantified using real-time PCR. Sequencing was performed on the MiSeq "Illumina" using the Kit v3 kit (300bp, paired-end read).

Metagenomic analyses. Sequencing data was analyzed using the Kaiju software, which allows for sensitive taxonomic classification of high-throughput sequencing of metagenomic or metatranscriptome samples [20].

Results and discussion. The multiple parallel sequencing of the genomic library isolated from the sample allowed to obtain a database of paired-end reads, each of which contained about 300 nucleotides. After bioinformatic processing of sequencing data, a database consisting of 658378 sequences belonging to three cellular domains and viruses was obtained. So, 75% of the sequences belonged to bacteria, 16% belonged to eukaryotes, and only 1% belonged to archaea. Viral sequences in investigated sample were identified in the amount of 7% (43009) (figure 2).

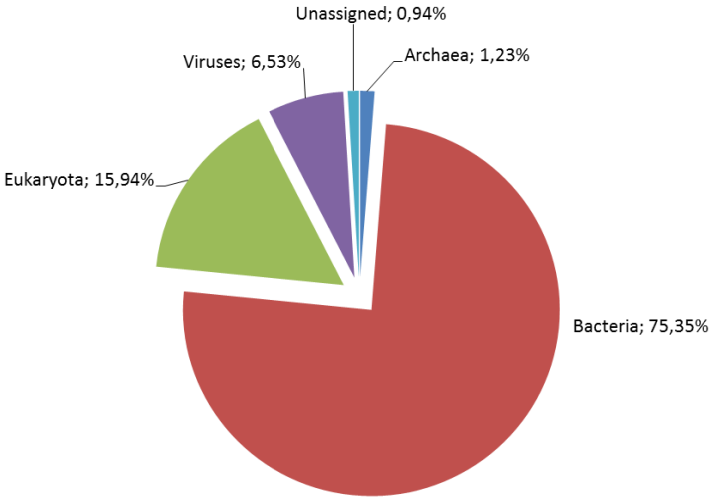


Figure 2 – The ratio of the number of sequences of the main domains

Of the 43009 viral sequences, viruses with different types of nucleic acid were identified, of which 65% were non-cultured phages and 26% were viruses with dsDNA genome (figure 3).

A comparative study of viral sequences and their belonging to host organisms showed that the dsDNA virome contains viruses of three large evolutionary domains: archaea, bacteria and eukaryotes, and consist of 3 orders, 19 families and a group of unclassified viruses (figure 4).

The dominant group of dsDNA virome were autochthonous prokaryotic viruses of the *Caudovirales* order (76%), as well as families of large nucleocytoplasmic DNA viruses, such as *Phycodnaviridae* (4.79%) and *Mimiviridae* (1.17%). Despite the apparently small number of viruses among the allochthonous viruses, 13 different families that can cause human and animal infections were detected, 2.5% of them were represented by the *Herpesvirales* order, *Iridoviridae* sequences were identified in the amount of 1%. Also there were sequences of unclassified dsDNA viruses in the amount of 11% in investigated sample (figure 4A) The remaining families capable of causing infections of humans, animals and plants were present in the water sample in an amount less than 1% (figure 4B).

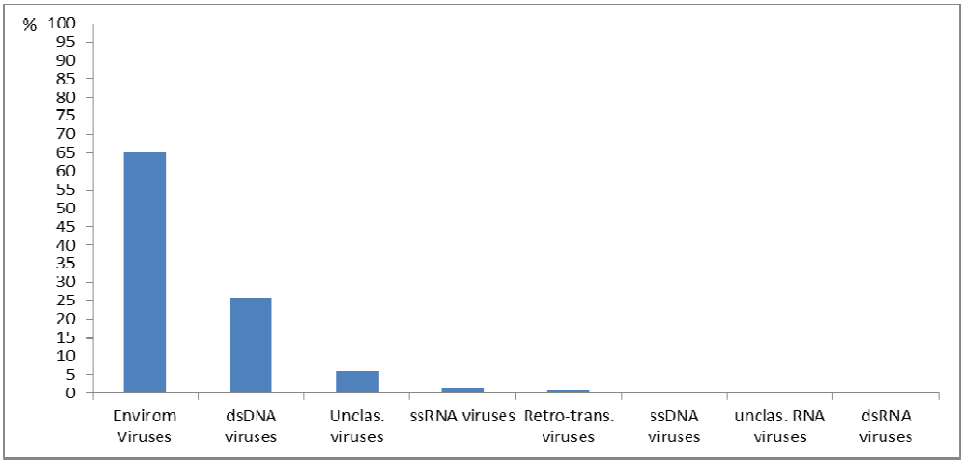
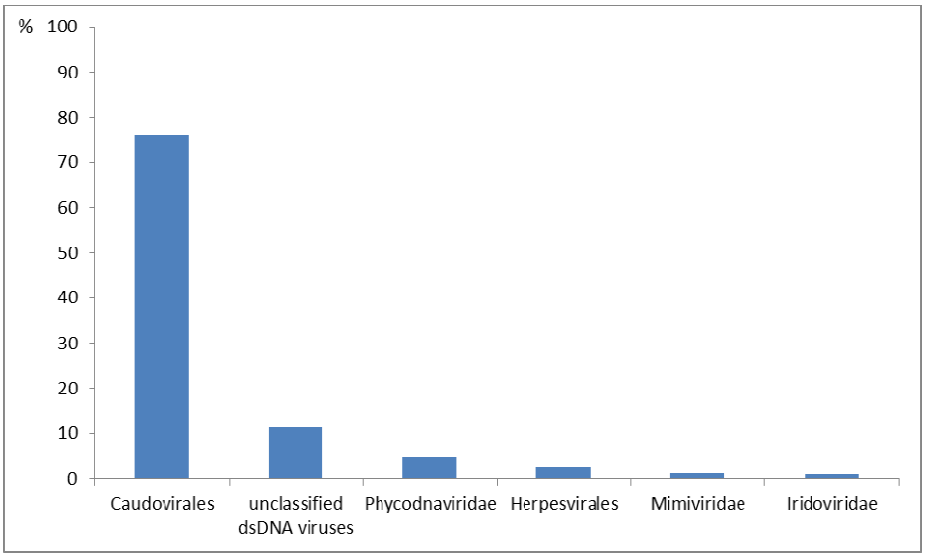


Figure 3 – The number of viral sequences with different types of nucleic acid



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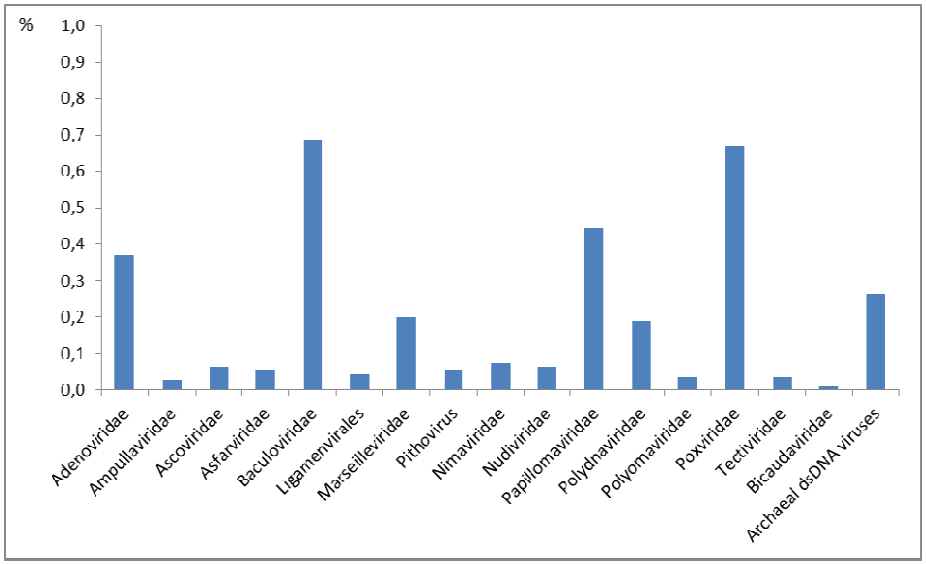


B

Figure 4 – Taxonomic composition of dsDNA virome

Among dsDNA viruses, tailed bacteriophages of the *Caudovirales* order, which contains the *Myoviridae, Siphoviridae* and *Podoviridae* families, were the dominant group (76%) in the surface waters of the Aral Sea. This result is similar to the findings of other marine viral metagenomic studies, such as Monterey Bay (65%), the Indian Ocean (95.3%), the Baltic Sea and the Antarctic Peninsula region of the Southern Ocean (~80%) in which these phages were numerically the dominant group [21-24]. *Caudovirales* were reported to infect a wide range of microbial hosts, including *Proteobacteria* and *Bacteroidetes*, which are dominant bacterial phyla in marine environments and therefore bacterial viruses (*Caudovirales* bacteriophages) are the most numerous in dsDNA virome in surface sample of the Small Aral Sea.

The percentage distribution of *Caudovirales* viruses in the studied sample was as follows: the *Podoviridae* family around 32.41%, *Siphoviridae* family around 25.38%, *Myoviridae* family 33.75% (figure 5). 9% were viruses not classified to the dsDNA family.

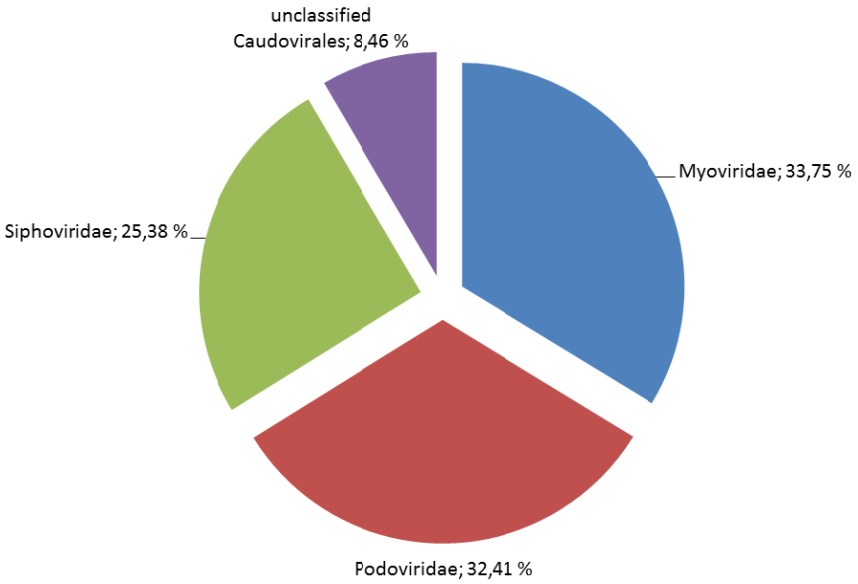


Figure 5 – Correlation of viral families of the *Caudovirales* order

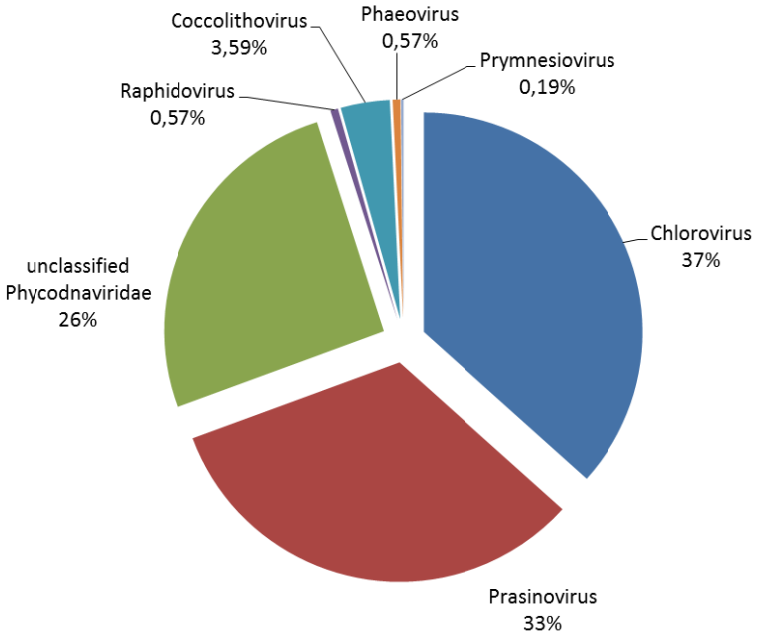
Nucleocytoplasmic DNA viruses were represented by *Phycodnaviridae* and *Mimiviridae* families.

Representatives of the *Phycodnaviridae* family that infect eukaryotic algae include the following virus genera: *Chlorovirus, Coccolithovirus, Phaeovirus, Prasinovirus, Prymnesiovirus,* and *Raphidovirus* [25]. Phylogenetic relationships between these genera are difficult to establish due to the lack of genetic data and a small number of characterized viruses in the family, which are less than three for each genus, except for *Chloroviruses*.

As a result of bioinformatic processing of sequencing data, the number of the *Phycodnaviridae* family representatives was about 5% of the total number of detected dsDNA viruses. In our sample, the sequences of all 6 genera of this family were identified, the most numerous were *Chlorovirus* genus (36.67%), Prasinovirus (32.70%), and representatives of unclassified *Phycodnaviridae* (25.71%). The remaining genera of this family were present in an amount of less than 1%: *Prymnesiovirus* (0.19%), *Phaeovirus* (0.57%), *Coccolithovirus* (3.59), *Raphidovirus* (0.57%) (figure 6).

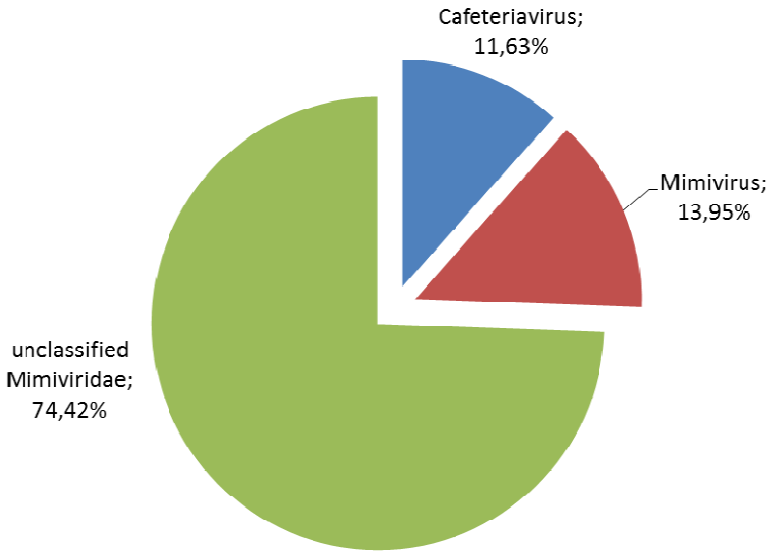
In addition, sequences of viruses infecting protozoa and belonging to the *Mimiviridae* family were identified. Recently, it was proposed to cluster mimiviruses into two genera: (1) *Mimivirus*: sub-divided into three non-taxonomical groups based on polB sequences: Group A (APMV and *Mamavirus*), Group B (*Moumouvirus*), Group C (*Megavirus chilensis*); and (2) *Cafeteriavirus*, which is a distant relation of the family *Mimiviridae* [26, 27]. In our sample, the *Mimiviridae* family was represented by *Cafeteriavirus viruses* (11.63%), *Mimivirus* (13.95%) and unclassified *Mimiviridae* (74.42%) (figure 7).

Unclassified viruses of the *Mimiviridae* family included representatives such as *Megavirus chiliensis*, *Moumouvirus*, *Niemeyer virus* and *Yellowstone lake mimivirus* in our sample.



Note. Data are given in% of the *Phycodnaviridae* family.

Figure 6 – Diversity of the *Phycodnaviridae* Family



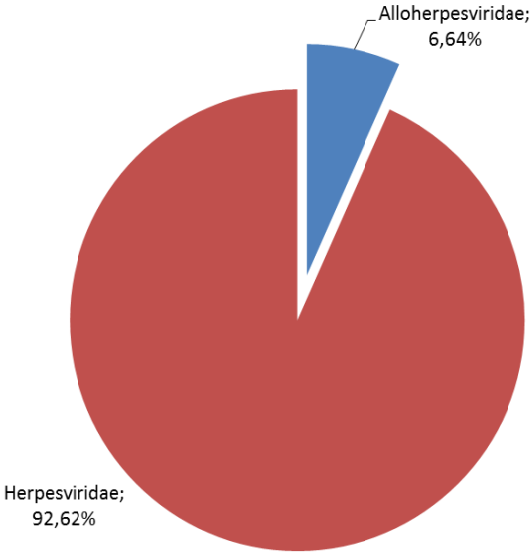
Note. Data are given in% of the *Mimiviridae* family.

Figure 7 – Diversity of the *Mimiviridae* family

In the studied reservoir, allochthonous viruses were represented by 10 families, the most numerous belonged to the *Herpesvirales* order and the *Iridoviridae* family.

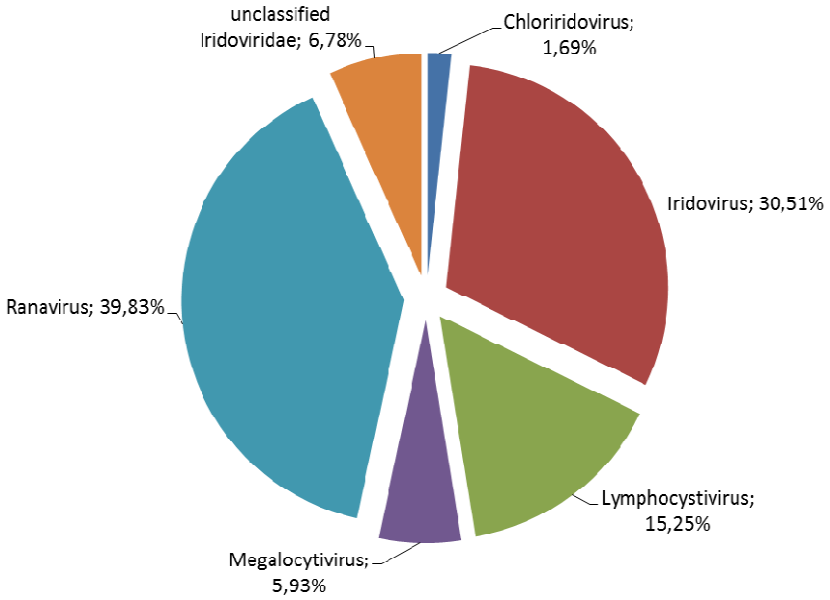
Herpesvirales is the order of DNA-containing viruses that cause a variety of diseases not only in humans and other mammals, but also in birds, reptiles, amphibians, fish. In the studied samples, this order was included two subfamilies *Herpesviridae* (93%) and *Alloherpesviridae* (7%) (figure 8).

Also, as a result of bioinformatics processing of metagenomic data, sequences of *Iridoviridae* viruses were identified, representing large icosahedral double-stranded DNA viruses that infect a wide range of both vertebrates and invertebrates (figure 9).



Note. Data are given in % of the *Herpesvirales* order.

Figure 8 – Representatives of the *Herpesvirales* order



Note. Data are given in % of the *Iridoviridae* family.

Figure 8 – Representatives of the *Iridoviridae family*

It was found that in the investigated samples identified *Iridoviridae* family consist of *Ranavirus* (40%), affecting amphibians; *Iridovirus* (30%), infecting mainly insects; *Lymphocystivirus* (15%) and *Megalocytivirus* (6%), whose host cells are fish, *Chloriridovirus* (2%), causing diseases of dipterous insects. In addition, *Scale drop disease virus* and *Anopheles minimus irodovirus* sequences related to unclassified viruses (7%) were present in the sample.

Conclusion. As a result of the research, the diversity of viral communities in the coastal waters of the Small Aral Sea was studied. It was shown that the double-stranded DNA virome of the sample contains viruses of three large evolutionary domains: archaea, bacteria, eukaryotes, and combines 3 orders, 19 families and a group of unclassified DNA viruses. It was also established that the dominant group of

dsDNA virome were autochthonous prokaryotic viruses of the *Caudovirales* order (76%), and families of large nucleocytoplasmic DNA of viruses, such as *Phycodnaviridae* (4.79%) and *Mimiviridae* (1.17%). Among the allochthonous viruses, 13 different viral families were detected, which accounted for approximately 4% of the total number of dsDNA sequences.

Thus, it was shown that autochthonous bacterial viruses represent the main virome of the sample, which indicates a rather diverse and developed population of prokaryotes in the Bolshoi Saryshyganak Bay of the Small Aral Sea. Such a population that has adapted to habitat conditions with a high salt content is the basis for the stable functioning of the local ecosystem.

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КІШІ АРАЛ ТЕҢІЗІНІҢ ЕКІ ТІЗБЕКТІ ДНҚ ВИРОМЫ

Аннотация. Қоршаған ортаның биоалуантүрлілігін зерттеу биологиялық пәндердегі зерттеулердің маңызды бағыты болып табылады. Әсіресе, тозған экожүйелерді зерттеу өзекті болып табылады, өйткені бұл экожүйенің тепе-теңдігін қалпына келтіру жөніндегі іс-қимыл бағытын көрсете алады. Мақалада Арал теңізіндегі екі тізбекті ДНҚ (дцДНҚ) виромның таксономиялық әртүрлілігі қарастырылады. Зерттеу объектісін таңдау ең алдымен дцДНҚ виромы кез келген экожүйенің ең көп құрамдас бөлігі болып табылады. Зерттелген үлгідегі виром көпше параллель секвенирлеу әдісімен зерттелді. Секвенирлеу деректерін өңдеу нәтижесінде 43009 вирусты тізбектер алынды. Вирусты тізбектерді салыстырмалы зерттеу көптеген вирустардың дцДНҚ – геномы бар екенін көрсетті. Виром дцДНҚ арасында автохтондық және аллохтондық вирустар бар екені анықталды. Ең көп болып *Caudovirales* және *Iridoviridae, Mimivridae* және *Phycodnaviridae* тұқымдастарының нуклеоцитоплазмалық вирустарына жататын үш эволюциялық домендердің ағзаларын зақымдайтын автохтонды вирустар болды. Санының аздығына қарамастан (3%) аллохтон вирустарының арасында адам мен жануарлардың инфекциясын тудыруға қабілетті 13 түрлі тұқымдастардың штаммдары диагностикаланды, бұл Арал теңізіне антропогендік әсер ететінін көрсетеді. Зерттеулер Арал теңізі вирустарының үлкен генотиптік әртүрлілігін көрсетеді,бұл әлемдегі ең көне тұзды су экожүйелерінің бірінде өмір сүретін вирустарды жан-жақты талдау қажеттілігіне әкеледі.

Түйін сөздер: Арал теңізі, виром, бактериофагтар.

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ДВУЦЕПОЧЕЧНЫЙ ДНК ВИРОМ МАЛОГО АРАЛЬСКОГО МОРЯ

Аннотация. Изучение биоразнообразия окружающей среды является важнейшим направлением исследований биологических дисциплин. Особенно актуальным является изучение деградирующих экосистем, так как это может указать направление действий по восстановлению равновесия экосистемы. В статье рассматривается таксономическое разнообразие двуцепочечного ДНК (дцДНК) вирома в Аральском море. Выбор объекта исследований обусловлен в первую очередь тем, что дцДНК виром любой экосистемы является самой многочисленной составляющей экосистемы. Виром исследуемого образца изучали методом множественного параллельного секвенирования. В результате обработки данных секвенирования было получено 43 009 вирусных последовательностей. Сравнительное изучение вирусных последовательностей показало, что большинство вирусов обладает дцДНК – геномом. Было установлено, что среди дцДНК вирома присутствуют как автохтонные, так и аллохтонные вирусы. Самыми многочисленными были автохтонные вирусы, поражающие организмы трех эволюционных доменов и принадлежащие к отряду *Caudovirales*

и нуклеоцитоплазматическим вирусам семейств *Iridoviridae, Mimiviridae* и *Phycodnaviridae*. Несмотря на кажущуюся малочисленность, (3%), среди аллохтонных вирусов диагностированы штаммы 13 различных семейств, способных вызывать инфекции человека и животных, что говорит об антропогенном влиянии на Аральское море. Исследования показывают большое генотипическое разнообразие вирусов Аральского моря, что подчеркивает необходимость всестороннего анализа тех вирусов, которые обитают в одной из древнейших в мире соленых водных экосистем.

Ключевые слова: Аральское море, виром, бактериофаги.

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