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Jüri TERAS, Leida KESA

THE RELATIONSHIPS BETWEEN PROTOZOA AND VIRUSES

2. VIRUS-LIKE PARTICLES AND CYTOPATHOGENIC AGENT IN PROTOZOA

As has already been mentioned in the first part of our paper (Teras, Kesa, 1988), in addition to endogenic viruses of protozoa which have been established only in *Entamoeba histolytica*, *Trichomonas vaginalis* and *Giardia lamblia* as yet, also virus-like particles (VLPs) or/and cytopathogenic, probably viral agent, have been found in some other protozoan species.

Up to now a most systematic and thorough study of these phenomena has been carried out in amoebae of *limax*-group, first of all *Naegleria gruberi* and *N. fowleri*, since some strains of these free-living protozoa inhabiting soil and water cause primary amoebic encephalitis usually ending lethally (Butt et al., 1968; Červa et al., 1968; Proca et al., 1973; Van den Driessche et al., 1973; De Jonckheere et al., 1974, 1975; Schuster, 1982).

It has repeatedly been suggested that the pathogenicity of free-living *limax*-group amoebae may be due to some factors inside them: either viruses (Schuster, 1969; Schuster, Dunnebacke, 1977), a cytopathogenic agent (Dunnebacke, Schuster, 1974, 1977*a*, *b*), or some other yet unknown endobiont (Proca-Ciobanu et al., 1975).

F. L. Schuster (1969) was the first to detect virus-like particles in *N. gruberi* while studying by electron microscopy the EGs strain, which, after eight years of axenic cultivation had been transferred to monoxenic cultivation. Immediately after that peculiar formations of ca 100 nm in diameter were detected in the nuclei of the amoebae of the monoxenic culture which the author named "particles of unknown origin". These particles, reminding, in the author's opinion, of reoviruses, contained an electron-dense nucleoid, which was surrounded by a membrane, covered by a layer of some diffuse material. Single particles could be seen also in the cytoplasm, being in close contact with tubular projection of the nucleic membrane. As was suggested by F. L. Schuster, such contact might refer to the transmission of virus-like particles from nucleus to cytoplasm.

Although this F. L. Schuster's observation had been occasional, it became a starting point for a number of further investigations together with T. H. Dunnebacke (Schuster, Dunnebacke 1971, 1974*a*, *b*, 1976, 1977; Dunnebacke, Schuster, 1971, 1972, 1974, 1977*a*, *b*, 1985) of the morphology and morphogenesis of VLPs in the organism of *N. gruberi*. By scrupulous electron-microscopy studies the authors established that VLPs can, first of all, be found in the nucleus of this protozoon. From there they move to the cytoplasm most probably through channels of nucleic membrane (Schuster, Dunnebacke, 1976). F. L. Schuster and T. H. Dunnebacke in their experiments with *N. gruberi* observed rupture of the nucleic membrane as it had been described by L. S. Diamond et al. (1972) in *E. histolytica* when the filamentous virus was released from the nucleus. Simul-

taneously the VLPs in the nucleoplasm of *N. gruberi*, the authors detected some fibrillar structures, and in the cytoplasm they found peculiar bodies reminding of bacteria, which might be associated with the formation of VLPs. These cytoplasmic bacteria-like formations were oblongate, 2 mkm in length and 0.5 mkm in width. When getting mature these bodies became round and spherical with a diameter of 600 to 900 nm (Schuster, Dunnebacke, 1971). In their earlier publications the authors supposed that the described particles were bacteria. But after a detailed investigation they came to a conclusion that these formations were transmissive structures of VLPs in their moving to other individuals in the culture. According to F. L. Schuster and T. H. Dunnebacke (1976) there is a rather close dynamic relationship between the formation of VLPs in the nucleus and associating with them bodies in the cytoplasm of *N. gruberi*. The authors are of the opinion that most probably the VLPs migrating from nucleus to cytoplasm become surrounded by membraneous structures there, which, when getting mature become round and engulf the VLPs, thus separating the latter from the cytoplasm. These newly formed spherical particles together with the VLPs migrate through amoebic cytoplasm to the medium where they can be engulfed by nutrient vacuoles of other amoebic individuals. Amoebae can be infected with VLPs also by fastening of spherical particles to the plastic membrane of amoebae, from where they move on into the cytoplasm, or else by phagocytosis of VLPs which have got into the medium after the rupture of spherical particles.

As F. L. Schuster and T. H. Dunnebacke (1974*a*, *b*) have ascertained in their experiments, formation of VLPs in the nucleus of *N. gruberi* depends upon the conditions of the cultivation of the amoebae. It appeared that in the amoebae, grown at 37 °C formation of VLPs in the first 12 hrs was much more abundant than in those incubated at 21°. But the next 12 hrs changed the picture totally: the number of VLPs in the amoebae, cultivated at 37°, abruptly dropped, whereas also transmissive bodies disappeared from the cytoplasm. At the same time some degenerative changes appeared in the nuclei of the amoebae as well as big clusters of fibrillar structures reminding of microtubes were found there.

As no such changes occurred in non-infected amoebae which had also been cultivated at 37°, the authors came to a conclusion that the established changes had been caused by the damaging effect of endobionts, i. e. VLPs in the nuclei of the amoebae, and not by elevated temperature.

Regardless of very intensive and thorough investigation of VLPs in the nucleus of *N. gruberi*, F. L. Schuster and T. H. Dunnebacke could not still ascertain the origin of these formations either by various cytological, virological or bacteriological methods. During their research, however, the authors gathered much information on the basis of which some quite reasonable surmises could be made. Thus, the authors draw our attention to the fact that, just like in L. S. Diamond's, C. F. T. Mattern's et al. experiments (Diamond et al., 1972; Mattern et al., 1972) with *Entamoeba histolytica*, the VLPs in *N. gruberi* in F. L. Schuster's (1969) tests were detected only after changes in the cultivation conditions of these protozoa. Viruses in *E. histolytica* were established after purifying the culture from associating microflora, and VLPs in *N. gruberi* — after transmission of cultures from axenic to monoxenic conditions. According to F. L. Schuster and T. H. Dunnebacke (1976) in both cases the changes in the nutrition and growth conditions were the necessary premise for manifestation of endobionts. The fact that VLPs in the axenic cultures of *N. gruberi* were observed neither in the nucleus nor in associating bodies in the cytoplasm brought F. L. Schuster (1969) to the thought that the formation of these particles might be induced with bacteria. Grounding on the results of further investigations F. L. Schuster and T. H. Dunnebacke (1976), how-

ever, expressed an opinion that VLPs exist in the nucleus latently and become manifest simultaneously with associating bodies in the cytoplasm only after certain metabolic changes. It was established that the number of amoebae with VLPs depends upon the ratio of amoebae to bacteria, since after the decrease of the bacterial admixture in the medium the VLPs appeared at first in the nucleus of some amoebae only (ca in 5 per cent), but at the further decrease of the amount of bacteria the number of amoebae with VLPs began constantly growing, reaching even as much as 50 per cent in the culture. At that in none of the experiments VLPs were observed in all the protozoa.

The formation or occurrence of VLPs was influenced also by other factors, whereas it was established that they appeared in the nucleus of amoebae even in axenic cultures when 5-bromodeoxyuridine had been added (Schuster, Dunnebacke, 1976; Schuster, Clemente, 1977). Thus the initial suggestion of F. L. Schuster's (1969) that the formation of these particles can be induced just with bacteria, which, most probably, play only the role of an inductor, was refuted.

As to VLPs in *N. gruberi* it should be mentioned that up to the present these formations have been found only in the nucleus of the amoeboid form of this protozoon, which, as is known, is able to be transformed into a flagellate one (Fulton, 1970; Page, 1974). Of most interest at that is the fact that the amoebae, infected with VLPs were never transformed into flagellate forms, nor were they ever encysted (Schuster, Dunnebacke, 1976). It is possible that this phenomenon was caused by the change in functional activity of *N. gruberi*, replicating and feeding only in an ameboid form (Yuyama, 1971). Taking into account the fact that the transformation process from an amoeboid to a flagellate form can be blocked by the inhibitors of RNA and DNA synthesis, it seems more probable that the synthesis of nucleic acids necessary for the transformation process is affected namely by nuclear VLPs. Beside VLPs in *N. gruberi* F. L. Schuster and T. H. Dunnebacke (1977) detected such particles also in the nuclei of MB-41 and Carter strains of *N. fowleri*, which turned out to be pathogenic for mice at intranasal inoculation of amoebic cultures. While studying the amoebae isolated from the brain of mice, which had died of experimentally caused amoebic encephalitis, the authors discovered clusters of the particles in the nuclei of the amoebae, not found in the protozoa used for infecting experimental animals. Some mice were observed to have such particles also in the nuclei of degenerated nerve cells, whereas the size of these particles in nuclei both of amoebae and nerve cells was ca 30 nm. In both cases the particles had no membrane or capside and differed apparently from the VLPs these authors had detected in *N. gruberi*. It is interesting to note that G. S. Visvesvara and C. S. Callaway (1974), who used the same strains of *N. fowleri* for infecting mice, found such particles neither in the nuclei of amoebae nor in the cells of experimental animals.

Entirely opposite results are presented by G. Carosi et al. (1977), who considered the presence of VLPs in the nuclei of the amoebae of *Naegleria* species so characteristic of them that on that basis they even distinguished between the afore-named species and amoebae of *Acanthamoeba*-group.

Alongside studies of the morphology of the VLPs in the nuclei of *N. gruberi* and *N. fowleri* attempts were made to ascertain their biological meaning and, first of all, their possible influence on the pathogenicity of amoebae. Already at the very initial stage of such investigations T. H. Dunnebacke and F. L. Schuster (1971) established that the lysates, devoid of cell, of EGs strain of *N. gruberi* cultures, in the nucleus of which the authors had detected VLPs, caused cytopathogenic changes in cultures of fibroblasts of chick embryos both at first infection and the follow-

ing passages. At the beginning the authors ascribed that action to VLPs, but when the lysates of the amoebic cultures of HB-1 strain as well as 4 strains isolated directly from water, in which electron-microscopy revealed no VLPs, gave analogical results, it became obvious that there was no such correlation (Dunnebacke, Schuster, 1974). The cytopathogenic agent reminding of animal viruses for its action on cell cultures of fibroblasts of chick embryos was later discovered also in 5 strains of *N. gruberi* and 4 pathogenic strains of *N. fowleri* but was absent from all the investigated strains of *Acanthamoeba astronyxis*, *A. castellani*, *A. culbertsoni*, *Polysphondylium pallidum* and *Didynium nigripes* (Dunnebacke, Schuster, 1974).

Proceeding from the obtained data the authors drew the conclusion that the presence of the cytopathogenic agent was connected with neither the appearance of VLPs nor the pathogenicity of strains but rather had something to do with the species of amoebae. The most surprising and unexpected for the authors was the fact that the cytopathogenic agent could be passaged on cell cultures of fibroblasts of chick embryos, and that the titre of this agent at passaging even increased. The further investigation of the cytopathogenic agent isolated from the lysates of the cultures of *N. gruberi* revealed that it was inactivated neither at repeated freeze-thawing, prolonged storage at −20 °C, nor under the influence of some detergents, and appeared to be resistant to the effect of proteases and nucleases, DNA-ses and RNA-ses, and to some extent, even to ultraviolet irradiation. The activity of the given cytopathogenic agent disappeared only after boiling and treatment with ureases (Dunnebacke, Schuster, 1977*a*, *b*, 1985).

Up to now the attempts to ascertain this agent by electron microscopy either in amoebae or cells of chick embryo, infected with it, have been unsuccessful. No better results have been achieved by trying to sediment this agent from infectious material by centrifugation 4 hrs at 100,000 g. On the basis of such data T. H. Dunnebacke and F. L. Schuster (1985) came to a conclusion that the detected cytopathogenic agent differed from all known viruses, reminding rather of scrapie agent for its properties.

These authors succeeded in isolating analogical cytopathogenic agents also from the lysates of the cultures of one pathogenic *N. fowleri* strain and two apathogenic strains of *N. gruberi* and *N. jadini*. These agents, too, proved to be transmissive on the cell cultures of fibroblasts of chick embryo, and were ascertained to have a molecular mass of only 50,000. This means that the cytopathogenic agent under investigation is much smaller than the smallest viruses known (Dunnebacke, Schuster, 1977*a*, *b*). Although the authors succeeded even in detecting proteins in the composition of this cytopathogenic agent, they did not regard it as a virus since they did not find any nucleic acids in it.

Therefore the origin of the cytopathogenic agent isolated amoebas of various species of *limax*-group by F. L. Schuster and T. H. Dunnebacke remains still unclear, as well as that of the scrapie agent. Despite that the authors are convinced that the pathogenesis of the primary amoebic meningoencephalitis is first of all connected with this agent, though they, like M. Proca-Ciobanu et al. (1975), do not deny either the possible role of VLPs in the transformation process of apathogenic strains of *N. gruberi* and *N. fowleri* into pathogenic ones, which cause amoebic meningoencephalitis in men.

As for another family of *limax*-group — *Hartmanellidae*, no viruses, VLPs or scrapie agent have been detected in them, as much as we know. One can find only occasional data in literature of cytoplasmic extramitochondrial DNA in amoeboid forms (Ito et al., 1969; McIntosh, Chang, 1971), the location of which has not yet been morphologically established.

Therefore, according to S. Ito et al. (1969), it should be related to the defective virus or else to an episome-like genetic element. Although no endobionts including bacterial ones have been found in the amoebae of the given family, some authors believe that the pathogenicity of strains of the free-living protozoon *Acanthamoeba castellani* can be explained just by the presence of endobionts in them (Proca-Ciobanu et al., 1975).

Beside the data on finding viruses (Diamond et al., 1972; Mattern et al., 1972; Diamond, Mattern, 1976) and VLPs (Schuster, 1969, 1973; Schuster, Dunnebacke, 1974*a*, *b*) in amoebae, one more frequently comes across recent reports in literature on detecting peculiar formations in malarial plasmodia, which are given various names — crystal protein inclusions, crystalloids, VLPs and particular inclusions.

The first to establish those unusual bodies in the organism of malarial plasmodia in *Plasmodium gallinaecum* (*Haemamoeba gallinacea*), isolated from hens and in *P. cynomolgi bastianellii*, isolated from monkeys, were the famous English protozoologist P. Garnham and his coworkers (Garnham, 1961; Garnham et al., 1962). By electron microscopy they discovered similar crystalloids in the cytoplasm of ookinetes of both species, which very much resembled the ECHO virus. These crystalloids were of irregular form, ca 1 mkm in width, with a diameter of 35 nm, and contained spherical bodies, which were covered by a membrane and consisted of a cluster of granules of different electron density. Although the structure of these crystalloids reminded very much of picornaviruses, the authors could not detect nucleic acids in them by histochemical methods and therefore did not regard them as viruses.

Some years later J. A. Terzakis (1969) also discovered VLPs in the ookinete of *P. gallinaceum*, but he used for his studies epithelial cells of the central intestine of the mosquitoes *Aedes aegypti*, infected with plasmodia, the development of which was restrained by the effect of the antimalarial preparation trimetaprim. The VLPs were 35—55 nm in size, included dense fine-granuled areas, were covered by a 5 nm thick trilaminar membrane and contained aggregates, which had 5.5 nm thick three-layer membrane. The described clusters appeared to be very similar to the crystalloids established by D. Garnham et al. (1962). In J. A. Terzakis' opinion they reminded of viruses, but as the classical Koch's postulate for proving this was not fulfilled, the author had to name these structures VLPs, although for some reasons he has entitled his article "A protozoan virus".

Later J. A. Terzakis, while investigating VLPs in malarial plasmodia, ascertained (Terzakis, 1972; Terzakis et al., 1976) that the crystalloid aggregates could lose their strict geometrical form. Separate particles of similar structure could be found in the cytoplasm, nucleus and even capsule of the oocysts. However, great variability in the sizes (from 28 to 67 nm), of separate particles of the aggregate was somewhat surprising for it is not typical of viruses. But taking into account the fact that in the negatively stained material, obtained by gradient centrifugation technique, VLPs of 42—45 nm in size had been observed, the authors attributed the dependence of the diameter of particles to their three-layer membrane or external cover missing in the particles of less diameter, which, most probably, appear to be incomplete or not yet mature.

The difference in the sizes of VLPs in *Plasmodii* was observed also by W. D. Trefiak and S. S. Desser (1973), but they gave an entirely different explanation to that. Namely, they supposed that smaller particles were formations of lipid-protein and only the larger ones, surrounded by membrane — viruses.

In *Plasmodii* there have been observed even bigger VLPs than those described by P. Garnham, J. A. Terzakis et al. It was ascertained that

identical formations can be found also in the organisms of the vectors of malarial parasites. Thus, E. E. Davies et al. (Davies et al., 1971; Davies, 1974) announced of detecting two different forms of VLPs in the epithelial cells of the central intestine of mosquitoes *Anopheles stephensi*, infected with strains of *Plasmodii berghei berghei* and *P. berghei nigeriensis*, cultivated at the laboratory. One of these forms — spherical bodies of 150 nm in diameter with a dense nucleotide of 70 nm in diameter, and surrounded by a membrane, — the authors detected also in oocysts of *Plasmodii*, whereas such particles appeared both separately and in clusters. Oocysts, which contained lots of such particles lacked the nucleus, their mitochondria were swollen and without typical electrondense matrix. In case of a smaller number of VLPs in oocysts the cytoplasm looked considerably desorganized, but the nucleus was there.

Although the size of the VLPs described by E. E. Davies et al. exceeded nearly three times that of the formations detected by P. Garnham et al. (1962) and J. A. Terzakis (1969), the researchers were sure of the identity of these particles, supposing that they have a somewhat damaging effect on the ookinetes of *Plasmodii*. P. Garnham et al. treated with caution the inclusions they discovered in the cytoplasm of ookinetes of *Plasmodii*, expressing even an opinion that these inclusions might be the reserve material of ookinetes, which is made use of during the development of oocysts. If the differentiation process of ookinetes-oocysts slackens down, the reserve material might appear not to be consumed up entirely.

Another group of investigators — R. G. Bird et al. — established VLPs simultaneously in the cells of adult mosquitoes (*Anopheles stephensi*) and in the cytoplasm of malarial *Plasmodium* (*Plasmodium berghei yoelii*) (Bird et al., 1972). At that it became evident that the epithelial cells of the central intestine, in which the inclusions of 54 nm in diameter as well as particles of 74 nm in size resembling typical polyhedral viruses were found, got destroyed. Identical VLPs lay in clusters both in vacuolized oocysts of *Plasmodii*, detected in epithelial cells of the central intestine of mosquitoes, and in some deformed and vacuolized sporozoites. Particles of 30 nm in diameter, which very much resembled polyhedral viruses, were found also in oocysts of *Plasmodium vivax* and cells of mosquitoes *Anopheles stephensi*, infected with those protozoa. L. S. Diamond and C. F. T. Mattern (1976) were rather critically minded with respect to these data as far as in the microphoto, displayed in the article by R. G. Bird et al., they saw no structures bearing any resemblance to viruses.

Other blood parasites have also been described as having formations, morphologically similar to VLPs but mainly, because nucleic acids could not be detected in them, these structures were not interpreted as being viruses (Desser, Trefiak, 1971; Gallucci, 1974).

As it appears from the above-mentioned data, the origin of VLPs, found in the organisms of *Plasmodii* as well as in the *limax*-group amoebae, still remains vague. Nevertheless, a number of interesting hypotheses have been put forward, thus encouraging to tackle this problem more intensively. In that respect the hypothesis of H. A. Dasgupta (1968, 1984) should be mentioned here, according to that the VLPs of *Plasmodii* can successfully be used in the fight against malaria as they have a damaging effect on both the protozoon itself and its carrier.

We cannot yet tell what is the practical importance of VLPs in protozoa, including *Plasmodii*. By far not all such formations need proof to be viruses, as for example the VLPs found in organisms of various species of *Paramecii* (Preer et al., 1953; Wichterman, 1953; Sonneborn, 1959; Ball, 1969; Beale et al., 1969). For instance, the microorganisms, detected in *Paramecium aurelia*, are identified at present as bacteria producing

a toxin, which has lethal effect on the sensitive strains of this protozoon (Preer et al., 1974; Осипов et al., 1976). In one of those endobionts, for a long time known as kappa-particle and now classified as *Caedobacter taeniospiralis*, production of toxin is connected with phage-like particles (Preer, Preer, 1967; Preer, Jurand, 1968; Preer et al., 1971).

All the known strains of *Caedobacter taeniospiralis* have phage-like structures, which, obviously, are not infectious. Usually these structures have a spherical, and at the same time often a hexagonal appearance, which refers to icosahedral symmetry. The diameter of these spherical forms is 50—120 nm, and sometimes they have tail-like structures. These spherical forms were isolated in the gradient of buoyant density of CsCl and DNA was established in them. More detailed data on these endobiotic bacteria of *Paramecii* as well as of other protozoa have been given in the articles published in 1985 in the Journal of Protozoology No. 3 (Corliss, 1985; Cavalier-Smith, Lee, 1985; Lee et al., 1985*a*, *b*; Reisser et al., 1985).

As can be seen from the above-given example, it is very difficult, if possible at all, to determine the origin of manifest VLPs by merely electron-microscope observations. Therefore we can speak of protozoan viruses only when it has been entirely proved. That is why one should have a critical mind as to the data concerning the findings of VLPs in unicellular organisms, although more often than not it may seem quite probable that they are really viruses.

Thus, for example, beside the above-mentioned interesting results of investigations of VLPs in organisms of *limax*-group amoebae and *Plasmodii*, in literature we can find descriptions of discovered formations of indistinct origin in the cytoplasm of the protomonad *Leishmania hertigi* (Molyneux. 1974; Croft, Molyneux. 1978, 1979; Molyneux, Heywood, 1984), in which electron-microscope studies revealed spherical virus-like particles of 55—60 nm in diameter lying in order typical of viruses. These particles had an external electron-dense membrane and electron-transparent nucleoid of 17—20 nm in diameter. Alongside these particles in the cytoplasm of *Leishmania* also stick-shaped structures could be observed, which, analogically to the spherical particles, had apparently no effect on the life cycle of this protozoon.

Since both detected formations manifested themselves in the cytoplasm of all dividing *Leishmania*, but ceased replicating when isolated from the organism of protozoa, D. H. Molyneux (1974) decided that he had been dealing with viruses.

It is highly probable, but still not yet definitely proved whether such supposable virus as in the given case or other similar cases is an endobiont of the protozoon, or it penetrates into its organism from the outside, using the protozoon in the future as a temporary or permanent host.

Therefore, speaking of protozoan viruses, one should bear in mind that this notion comprises the viruses, adapted to replication and persistence only in unicellular organisms, but not all the viruses, which can be found in protozoa, since in the latter also mammalian viruses can replicate, persist and inactivate.

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Academy of Sciences of the Estonian SSR,
Institute of Experimental Biology

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Jüri TERAS, Leida KESA

ALGLOOMADE JA VIIRUSTE VAHEKORD

2. Viirusesarnased partiklid ja tsütopatogeenne materjal algloomades

Lisaks algloomade endogeensetele viirustele (Teras, Kesa, 1988) on algloomades leitud ka viirusesarnaseid partikleid ja tsütopatogeenset, tõenäoliselt viirusliku päritoluga materjali. Mõlemat fenomeni on senini põhjalikult ja järjekindlalt uuritud vaid nn. *limax*-grupi amööbidel ja seda eelkõige seetõttu, et kahe sellesse vabalt elavate algloomade gruppi kuuluva, mullas ja vees elava ainult apatogeensena tuntud liigi — *Naegleria gruberi* ja *N. fowleri* mõned tüved on osutunud inimestele peaaegu eranditult surmaga lõppeva nn. primaarse amöbiaalse meningoentsefaliidi tekitajaiks.

Korduvalt on kirjanduses väljendatud arvamust, et *limax*-grupi vabalt elavate amööbide patogeensus on tingitud kas viirustest, tsütopatogeensest materjalist või mingist senitundmatust endobiondist.

Kõrvuti selliste andmetega *limax*-grupi amööbide kohta leidub kirjanduses teateid ebatavalistest, kristalseteks valgulisteks kehakesteks, kristalloidideks, viirusesarnasteks partikliteks või partikulaarseteks kehakesteks nimetatud moodustistest ka malaaria plasmoodiumides. Samuti on ebaselge päritoluga moodustisi kirjeldatud ka *Leishmania hertigi* promastigootide tsütoplasmas, kus elektronmikroskoopilisel uurimisel sedastati sfäärilisi viirusesarnaseid 55—60 nm suurusi viirustele iseloomuliku paigutusega partikleid. Peale selliste moodustiste on leišmaaniate tsütoplasmas täheldatud pulgasarnaseid struktuure, mis nagu sfäärilised moodustisedki ei näi mõjutavat algloomade selle liigi elutegevust. Paraku ei ole senini suudetud selgitada, kas ainuraksete organismis sedastatud viirusesarnased partiklid on algloomade endobiondid või on nad sattunud algloomadesse ümbritsevast keskkonnast ja kasutavad neid kui reservuaare.

Rääkides nii algloomades leiduvatest viirustest kui ka viirusesarnastest partiklitest, tuleb alati arvestada võimalust, et tegemist ei ole mitte ainult algloomade endogeensete viirustega, s. t. viirustega, mis on replitseerumisvõimelised ainult ainuraksetes organismides, vaid ka imetajate, lindude, kalade ja taimede keskkonda sattunud viirustega, mis on persisteerimis- või replikatsioonivõimelised ka algloomades.

Юри ТЕРАС, Лейда КЕСА

ВЗАИМООТНОШЕНИЕ МЕЖДУ ПРОСТЕЙШИМИ И ВИРУСАМИ

2. Вирусоподобные частицы и цитопатогенные агенты в простейших

У некоторых видов одноклеточных организмов найдены кроме эндогенных вирусов (Teras, Kesa, 1988) вирусоподобные частицы или/и цитопатогенные, по всей вероятности, вирусного происхождения агенты.

До настоящего времени более последовательно и систематично эти феномены исследованы у амеб группы *limax* и, прежде всего, *Naegleria gruberi* и *N. fowleri*, так как некоторые штаммы этих свободноживущих простейших, обитающих в почве и воде, являются возбудителями первичного амебного менингоэнцефалита, имеющего обычно летальный исход. Неоднократно высказывалось мнение, что патогенность этих амеб может быть связана с наличием в них либо вирусов, либо цитопатогенного агента, либо какого-то еще неизвестного эндобионта.

Наряду с данными об амебах группы *limax*, в литературе встречаются сообщения о нахождении в малярийных плазмодиях необычных образований, которые имеют самые различные названия, такие, например, как кристаллические протеиновые включения, кристаллоиды, вирусоподобные частицы, партикулярные включения.

Имеются также сведения об обнаружении образований неясной природы в цитоплазме промастигот *Leishmania hertigi*, в которых при электронно-микроскопическом исследовании были найдены сферические вирусоподобные частицы диаметром 55—60 нм, расположенные в типичном для вирусов порядке. Кроме этих частиц в цитоплазме лейшманий наблюдались еще и палочкообразные структуры, которые подобно сферическим частицам на жизнедеятельность данного простейшего, по-видимому, не влияли.

Являются ли вирусоподобные частицы и цитопатогенные агенты, установленные в организме простейших, эндобионтами одноклеточных организмов или проникают в них извне, используя в дальнейшем простейшее как временного или постоянного хозяина, до настоящего времени выяснить не удалось. Однако следует иметь в виду, что среди них могут быть и вирусы млекопитающих, птиц, рыб и растений, которые приспособились к репликации и персистенции в организме простейших.