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Short Communication

Modern ideas About Association Virus A Flu with cell Komponetami (Literary Review)

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Most of the known modern structural models of influenza virus are based on molecular-biological, electron-microscopic and other methods of research and boil down to the description of known constituent components of a viral particle, place of their localization in virione and explanation of the established or intended functions.

However, based on the description of the presented generalized modern models of the influenza virus, we do not easily calculate a number of very important in structural and functional aspects of the virion, which are: DCell membrane [1-3], group antigen [4], Specialicethesi antigen, GeteroloForsmana [5,6], ATP-ase [7], ADP-ASE, Lecytinase [8,9], tripsinopodobnaya hroteaza [10,11], Carboxypeptidasa in [12], RNA-a, [13], lipids [14], carbohydrates [15], ovalbumin [16,17], hemolysis, most of which are cellular components of the influenza virus. These are antigens, enzymes, and other components of the influenza virus that have a cellular origin but are found in a viral particle.

So far, at least 13 computers have been detected as part of the viral particleof cellular nature [1-4, 20-22].

First of all, it is a compulsory part of viriona – double-layer lipid membrane – derivate cell membrane, which in weight is 24% of the virus weight. The lipid component of mixsovyruss, according to various researchers, is 18,5-37,5% of the total weight of virion (Koayakov P. N, 1970). These lipids are represented by phospholipids, glycolipides, proteolipides, cholesterol and neutral fats and contain a comparatively large count arginine and methionine [13].

It remains debatable to what extent this lipid membrane is modified by the virus or its constituent parts when the virus exits the cell. Most specialists believe that this is a derivate cell membrane. In its modification important participation takes viral neurominiidas, which splits from cell lipid receptors neuruminovuyu acid. It is due to the presence of the lipid membrane the structure of the virus and the installation of all its components. Glycoproteids-hemagglutinin and neurominiidas are placed on the surface of the lipid membrane, and all other viral proteins and RNA enclosed Inside lIpidnoj shell [21,22].

On the known models of the flu virus, as well as other shell viruses, the lipid membrane is presented structurally with the designation of its localization location and the intended outlines. As for other components of the influenza virus of a cellular origin, no known model of influenza virus does not take them into account. Neither antigens nor enzymes of the virus that have a cellular origin are taken into account.

This is probably due either to the fact that a number of components are represented in a small number, or to the fact that, according to modern data, these components do not represent a significant contribution both to the structure of the virus and its functional relationship in Process of viral reproduction. However, the analysis of the accumulated information forces to reconsider the established representations.

Laver W.G. и Webster R.G. [23,24] indicate that "although the first descriptions of the antigen of the host cell in the influenza virus were met with some scepticism, at present their existence is established firmly".

The first serological searches of the host cell antigens in the influenza virus belong Knight C.A. (1944) и Cohen S.S. (1944) [25].

These researches are summarized in the monograph of P. N. Kosyakov and Z. I. Rovnova (1972), and now it is possible to conclude, that in structure of the cleared influenza virus the antigenic components common with antigens of the owner's cage are long discovered: it is heterogeneous antigen Forsman; antigen, similar to the group specific antigen A and human; antigens, bearing the species specificity of those cells, nand which in the virus multiplies [18,19].

Later, the same antigens were found in other shell viruses – orto and parammiksoviruses.

As for their localization, it is known that an antigen similar to a group specific antigen A is not located in the outer shell of the virus. For its detection it is necessary to carry out deep destruction of virions by spirit and ether, to concentrate lipid extracts.

The specific antigen was found in the same virus, grown on cells of different species, in the RSK with the specific serum. It was found that the peculiar antigen of the hostPotassium in the in V-antigen, and in the nucleoproteid fraction of the virus (in S-antigen), the master's species antigens were not detected.

The antigen of Forsman was also found in the V-antigen mixsovviruses, i.e. in the outer shell of the virion, while the virus nucleoproteid did not contain it. Consequently, the Forsman antigen in the influenza virus is located more deeply than in the Sendai and Newcastle viruses. Antigen Forsman is a glycolisid common to many living cells and is reported in the serological reaction of passive agglutination with tissue antigens (RDPA) with serum, obtained by immunization of animals with tissue antigens. The adsorption of these serum rams of RAM completely removes antibodies against Forsman's antigen.

It is generally accepted that mixsovirus go out of the cage gradually by budding. This is typical for viruses: influenza, parainfluenza, avian leukemia, Rausa sarcoma, herpes group (herpes b and simple), some arboviruses (equine encephalitis).

The "protrusion" of the cellular protoplasm enclose the units of the virions, which are detached from the cells together with the fragments of the cell membrane, taking away the areas of cellular cytoplasm. As a result of the very mechanism of releasing the influenza virus from the cell, the virus is constantly enriched with composite cell components.

However, recognition of this view does not imply, as P. N. Kosjakov believes, the mechanical involvement of cell mThe structure of the viriona [18].

After establishing the fact of belonging of the named cell antigens to the viral particle, the question arose about the value of cell antigens in the composition of viruses for the development of infection and immunity, as well as the possible role in the manifestation of biological properties of viruses.

It has been established that anti-outbreaks applied to the three host antigens found in the influenza virus cause or completely neutralize the infectious properties of the virus, or the reduced ability to form hemagglutinin in Infected chicken embryo. That is, antibodies to cells have a direct effect on the activity of the virus containing the corresponding antigens of cells. At the same time, the more the cell antigen is superficially located in a viral particle, the more active are antibodies. For example, the antigen of Forsman in the influenza virus, according to P. N. The, is localized deeper than the specific antigen and, accordingly, anti-serum to it have less viral neutralizing activity.

Recently, in the preparations of shell RNA-containing viruses found a large number of different kinds of enzymatic activities: Kynazna, Phosphatazazna, polymerase (nucleic acids), nuclease and some others. It was difficult to explain the presence of activities due to contamination of viruses by extraneous materials, at least in some cases, as data indicating the internal localization of enzymes in viral particles were obtained. A variety of activities makes it unlikely and viral backgroundsf corresponding Enzymes [25].

For the first time, the proteincinase activity was found in purified drugs Onkoron-and Rabdovyruss (Strand m., August J.T., 1971). Soon there were other reports of phosphorylation of proteins of some viruses in cells and non-cellular systems (Sokol F., Clark H.F., 1973, etc.). A fundamental study of the subject was undertaken by Imblum R.L. and Wagner R.R. (1974). The authors have found that all studied vesicular stomatitis Virus, grown in five different cell lines, including animal, human and insect cells, contain proteinkinase activity and that to detect activity required Treatment of the viral drug by detergents. At comparison of some kinetic parameters authors have found out a difference of these parameters in preparations grown in different hosts, and also considerable similarity of optimums of detection of activity of the virus and cages in which the given preparation has been grown. At fractionation of viral particles in all cases the maximum of activity was observed in fractions enriched by internal protein LIPOPROTEIDNYH membranes Virionov (protein m), which implied either a similar localization of enzymes with protein m, or enzymatic the nature of the protein M. With the help of chromatography on the column with cellulose phosphate managed to separate enzymatic activity from the main mass of protein m. The authors have concluded about the cellular nature proteinkinase virus vesicular stomatitis (Air Force) and the localization of the enzyme in the area of the inner layer of the viral membrane.

The data of more direct experiments aimed at search of cellular proteins in the composition of viral particles were recently published. The proteins of the cells were methyl-amino acids, then infected with the Sendai virus, and the proteins of infected cells were methyl-amino acids. The virus, grown in these conditions, was cleaned, and the proteins of the purified drug were analysed with the help of electrophoresis in Polyacrylamide Gel (PAAG). The ratio of tritium and radioactive carbon was determined in the gel

fractions. In all detected components, this ratio of BMore or less Posto (circa 100). In only one class (so-called protein 7) it was sharply reduced (up to 12), which obviously pointed to the significant predominance in this material of protein molecules formed before the infection, i.e. cellular. When comparing the composition of proteins of the virus and unwound cells in the latter, the dominant component, electroforetically identical to Protein 7, was discovered. The authors made a conclusion about the cellof protein 7 viral particles [26].

Several earlier Op Zhirnov and co-authors (1974) among minor proteins in the purified product of the Sendai virus found a component, electroforetically similar to protein 7, received by American researchers. In this work the internal localization in viral particles of protein-analogue protein 7 has been established. Interestingly, the electroforetically identical class of protein molecules was found in the preparations of onkoronviruses and in manyTheir animal cages [2]. If it is not a simple coincidence, such result can speak about natural receipt of identical or similar for cages of different origin of proteins in structure of shell RNA-containing viruses.

It should be noted that the issue of the inclusion of host proteins in large RNA-containing viruses has a rather long history. It began with the detection of viruses en of the master's determinant [19]. Sometimes such results were treated as an indication of the presence of host proteins in viral particles. This viewpoint has been criticized for at least three reasons. First, the concept of antigen and protein are not identical. Secondly, one of variants of origin of antigens of the owner seemed obvious: the use of cellular Glycolyltransferaz for glycolylation of proteins of spikes could lead to formation of oligosacharid blocks of molecules of proteins HN and F, bearing cellular Antigenic specificity. Thirdly, there was an opinion that the presence of cellular proteins in the preparation of the virus is a consequence of either insufficient purification, or indifferent to the virus of sorption of cellular proteins on the surface of the virion. Several papers were published, the results of which this opinion [19].

Now there is a reason to believe that cellular proteins can still be included in viral particles. Since cellular proteins are contained in relatively low concentrations, for their detection requires the use of special methods (identification of enzyme activity, coelectrophoresis of cellular and viral proteins, labeled with different isotopes). However, it should be noted that the inclusion of host proteins as antigens (this issue was repeatedly discussed) may have a limited meaning. Currently available data suggest the internal localization of cellular proteins in virione. It is unlikely that the internal proteins can be recognizable or not recognizable by immune systems, as in the viral particle they are reliably screened by lipids and their demasking is possible only inside the infected cells, where the possibilities for their recognition sharply Limited. The other thing is the proteins of the host, localizable on the surface of the virion.

The most interesting and promising area in the study of the influenza virus, which is booming and growing in the last decade, and which has largely determined the progress of our knowledge in explaining the biological functions of the influenza virus as infectious, pathogenesis, virulence and others, is the study of the role of the system of cellular proteases and their inhibitors in influenza.

As part of the purified influenza virus, proteolytic enzymes were first discovered by J. J. Holland so on. In 1972 [28]. The authors identified the proteiases associated with the influenza virus but could not decide on the source of their origin and equally assumed the possibility of their viral and cellular origin.

And, before the nature was established and some functions associated with the purified proteinase influenza virus and evidence of its cellular origin were obtained, varied studies were carried out For Abroad and in our country [11,23,29].

Close attention to the role of proteolytic enzymes in influenza was drawn after the academician V.M. Zhanovym in 1961 possible mechanism proteolytic deproteinization virus Influenza [30], as well as after accumulating numerous data on increasing the yields of various viruses under the influence of small concentrations of trypsin culture [31]. These materials were first summarized in the review of V. P. Lositsky and. I. Degtyarenko [32].

In 1971, the domestic scientists e.v. Arkhangelsky, P. N. Kosjakovym, A.V. Bobov (1971) and Ni Milovidova (1974) [33- 34]. Studies of the role of Proteinaz and their inhibitors in influenza, which resulted in the presence of a vaccine-related Tripsionodobnoy proteinase, which was similar to the same Tripsionodobnoy proteinase. Plasmatic Membranes En kFlying light white Mice [35].

Here it is necessary to specify that data on splitting of viral hemagglutinin (on) on two polypeptides on HA 1 and HA 2 and on presence of them in influenza virus, S. G. Lazarovich and co-authors ofIn 1971 [36]. However, the same authors also disoriented researchers with their first reports on the issue in 1973, reporting that splitting into two polypeptides does not affect infectious Properties of the influenza virus [36]. This circumstance was rightly noticed by A.G. Bukrinskaya-sponsored in 1978 [26], which indicated that as early as 1975 the works of Klenk H.-D. Al and Lazarowitz S.G., *et al.* was refuted this is a mistaken view [37].

In 1980-1983, we and the group V.P. Lositsky were in parallel conducted studies on the nature of Proteinase and the role played by Proteinaza cells in the pathogenesis (virulence, infection) influenza and other its functions. It was concluded that Proteinas is necessary for realization of information potenations of Vironic RNA and viral polypeptides [11,38].

All of this applies equally to cellular proteiase associated with the influenza virus.

The analysis of the methodical part of the executed works testifies that the majority of the researches carried out in this direction are executed on the preparations of the virus, repeatedly purified chromatographic, re-adsorption and enlition on erythrocytes, Repeated ultra-centrifugation in radial density sugar [39-42]. Moreover, there were some works that confirm that it is impossible to make the separation of the components of the host from the influenza virus polypeptides practically even under the condition of the use of powerful detergents-tvin-80 and ether, 8-Octilglukyzida, Sodium DHA, Tritona X-100 and a number of others [43,44].

Therefore, we think it is time to get rid of those unfounded arguments that the cell components in the viriona are caused by an artifact or methodical errors. Of course, modern methods of molecular biology and chemistry allow to artificially disputation any chemical complexes or compounds available in the Virione, however, in natural conditions such chemical technology is excluded. Skepticism with regard to the cellular components of the influenza virus has finally passed with the publication of works on the role of Proteinaz in the splitting of viral structural glycoproteides-predecessors, as well as the ability to block infectious properties of influenza virus Specific inhibitors Tripsinosodobnogo proteiase of cellular origin and implement directed influenza therapy, which is based on pathogenetic and etiotropic action.

We have long drawn attention to the fact that the concentration and purification of the influenza virus leads to increased proteolytic activity in the preparations of purified and concentrated influenza virus, resulting in specific proteolytic activity per 1 mg Protein has risen sharply. Similar phenomenon was found by O. P. Zhirnov and A.G. Bukrynskaya (1977g.) in the purifiedThe Sendai virus Preparations [45,46]. It is also established that the activation of proteolysis is observed in the preparat purified foot-and-mouth disease. O. P. Zhirnov, A.G. Bukrynskaya and A.V. Ovcharenko suggested that during the purification process inhibitors of proteases are removed, which causes the increase of proteolytic activity in the Prepare purified foot-and-mouth disease [47]. Rapid activation of proteolysis as a result of direct contact of the preparations of the purified influenza virus with purified high-speed centrifugation by plasmatic membranes sensitive to the influenza virus of light white mice cells was found by V.I. Degtyarenko and V.A. Lositsky in 1977 [48].

Currently, there is no complete information on the list of the owner's cell antigens in the influenza virus, their number and functional biological activity. Difficulties In their study, except those mentioned above, are also caused by small quantitative content of them as a part of a viral particle. However, small quantitative content does not speak about anything, especially, if it is about the proteins of the owner, performing highly specific enzyme functions.

In the light of these literature, as well as our own, the model of a functioning influenza virus should be constructed taking into account all known components of the Viron and should therefore contain a well-known list of "master" cell proteins, carbohydrates, Lipids that the influenza virus receives from the host cell in the process of budding from the surface of the plasmatic membrane and without which it is impossible to even imagine the normal physiology of the influenza virus.

At deproteinization of shell viruses and, including, influenza virus, shell components of a virus and cages are mutually merged and constituent parts of them somehow, yet precisely not known way, are mutually redistributed among themselves, becoming a uniform Membrane, making the contents of the virus included in the cell's cytoplasm. Therefore, the concept of "deproteinization" remained essentially unchanged and, in this regard, is competent to assert that cellular protease carry out deproteinization of influenza virus, KATo it asserted V.M. Zhdanov [30].

Methodological approaches to the interpretation of the role of Tripsionodobnoy proteiase associated with the virus, acquire new illumination, because they make very strictly approach to all kinds of molecular-biological United Nations Explanations of structure and Influenza virus, which were carried out without taking into account the presence of the master cell components with high enzymatic activity and molecular heterogeneity. Since without this consideration it is not possible to properly assess the ecology of the influenza virus, its variability, adaptive adaptability, the ability to chronic persistence, etc. This article the literature on the nature of Tripsionlike proteiase associated with the influenza virus has been summarized, justifying the need for our Research in this area.

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