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BIOTECHNOLOGICAL RESEARCH IN THE CREATION AND PRODUCTION OF ANTIRABIC VACCINES

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Rabies is a neurological disease of a viral nature, leading to death. Rabies virus is an RNA virus that invades the central nervous system, leading to neuronal dysfunction. Timely vaccination can prevent the diseases development.

Aim. The article is devoted to immunobiotechnological research aimed at creating antirabic vaccines.

Results. The history of the antirabic vaccines creation from the first inactivated vaccines obtained from nervous tissue to the cultivation of the virus on animal cell cultures is considered. The article presents commercially available anti-rabies vaccines: their composition, the used rabies virus strains, cell cultures, the methods of inactivation and purification. The technology of producing an anti-rabies vaccine based on a Pitman Moore virus strain and a chicken fibroblast cell culture is presented. The advantages of different vaccine types are considered: live attenuated, peptide, liposomal, RNA vaccines, vaccines based on viral vectors, transgenic plants and reverse genetics methods.

Conclusions. The development of biotechnology, immunology and virology makes it possible to improve constantly vaccine preparations, including those against rabies, increasing their effectiveness and safety.

Key words: immunobiotechnology; viral vaccines; antirabic vaccine; RNA virus; rabies virus.

Rabies (R) is one of the oldest neurological diseases caused by the rabies virus — *Rabdovirus* (RV). The virus belongs to the genus *Lyssavirus*, the *Rhabdoviridae* family. RV is a neurotropic, RNA negative single-stranded virus. RV causes a lethal encephalitis in mammals known as R, which causes 60,000 deaths worldwide annually, leading to death with the development of clinical symptoms. In Ukraine, 20894 people were vaccinated in 2019, 1938 of them were with a confirmed R diagnosis [1]. The virus enters the peripheral area after exposure and subsequently spreads to the central nervous system, causing neuronal dysfunction, which is the main cause of death in R [2].

All Rhabdoviruses have 2 main structural components: the helical nucleoprotein nucleus (RNP) and the surrounding envelope. The RV genome encodes five proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G), polymerase (L). G forms about 400 spines densely located on the viral surface. Protein M is associated with both envelope and RNP and may be the central protein of the RV assembly (Fig. 1).

RV enters the nervous system by binding to nerve receptors such as acetylcholine, nerve cell adhesion, nerve growth factor receptors. The RV is then transported to the central nervous system by axonal (retrograde) transport, possibly by binding to cytoplasmic dynein. In axons, RV carries out retrograde transport by means of movement on the cytoskeleton tubes surface — they move from the plus-ends to the minus-ends (Fig. 2).

G, the only protein exposed on the surface of virions, is the main viral component responsible for the induction of host antibodies. G serves as an important vaccine immunogen (Vac) against R. Various constructs expressing protein-G are being developed using paramyxoviruses and adenovirus vectors that can induce sustained humoral immunity in the RV response [4].

Immunobiotechnology, in particular, vaccinology, enables to prevent the disease R with the help of vaccination, provided that it is carried out in a timely and correct manner.

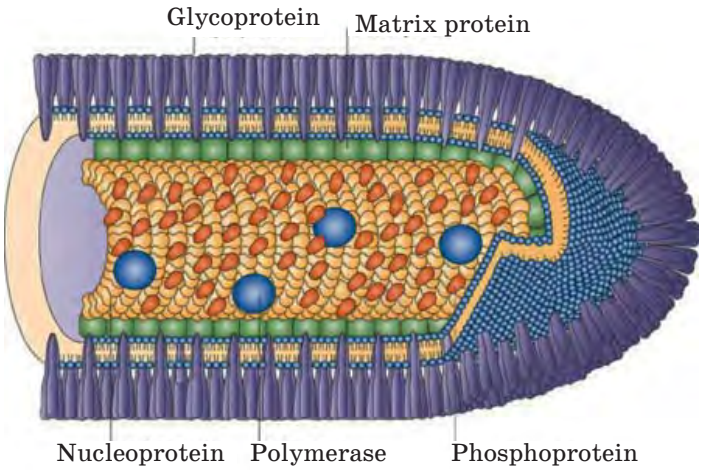

Fig. 1. **Schematic structure of the RV virion [3]**

Since the time of Louis Pasteur (1822–1895), Vacs for human versus R are made from inactivated RV. Since 1880, L. Pasteur began the experimentations aimed at artificially reducing the virulence of infectious agents and obtaining attenuated strains. He obtained weakened pathogen strains of chicken cholera and anthrax. L. Pasteur used the principles and methods of attenuation upon Vac against R receipt and practical use. Having received the so-called fixed RV (fixeRV) with a standard virulence degree, Pasteur injected RV suboccipitally into rabbits, causing them to become infected. Then the spinal cord of the animals was subjected to drying at different times, which caused RV attenuation and a decrease in the number of living RV particles. This research led to the creation of the anti-rabies Vac (antiRab-Vac). L. Pasteur applied his discoveries well beyond the animals, but to humans: a boy was brought to him from Alsace, who was bitten by a mad dog. Pasteur began a course of 13 injections of emulsified rabbit spinal cord material three days after the child was bitten. 90 passages were used by L. Pasteur for the first Vac with Virus Fixe. Vac against RV developed by L. Pasteur was obtained from neural tissue, and RV was inactivated by drying. However, this Vac posed a danger according to the possibility of RV activation and the development of allergic reactions due to the presence of myelin in the nervous tissue. For the first time, vaccination against R was carried out using the brain Vac, registered by L. Pasteur in 1885. Later, the safety of Vac was increased by phenol inactivation of RV (1911). However, after use, serious side effects were still observed, including several cases of paralysis and death. The main factor is hypersensitivity to myelin. Subsequently, it has been found that the amount of myelin in Vac could be reduced by using neonatal mice with lower myelin levels in the brain [6].

In Ukraine, until the early 80s, a lyophilized antiRab-Vac of the Fermi type, made from the brain of infected with Virus Fixe sheep, was used. The homogenized brain in a 0.9% NaCl solution containing 1.0% of phenol was inactivated for 8 days at a temperature of 20–22 °C. Sucrose is added to Vac and the mixture is lyophilized. Serious side effects associated with hypersensitivity to myelin were observed with Vac application. In addition, it is necessary to take into account the presence of various immunochemically active lipids in the brain Fermi Vac [7], which can lead to the appearance of anti-lipid antibodies [8]. It should be noted that the brain tissue contains gangliosides (Gan), which can serve as receptors for binding to RV. The study of Gan isolated from the cattle brain (GT1 and GD1a) in *in vitro* and *in vivo* experiments showed antiviral activity when infected with RV in animals at the early stages of infection. The survival value in comparison with the control (death of 100% of animals) ranged from 20 to 60% (virus activity was 50–100 LD_{50}), depending on the concentration of Gan [9].

As it can be seen from the above data, antiRab-Vac was originally obtained from neural tissue. Currently antiRab-Vacs are mainly Vacs based on cell cultures and avian embryos. In subsequent years, the specialists were faced with the task of creating antiRab-Vac production on biological substrates free from nervous tissue. Vacs began to be obtained on the basis of cell cultures of avian embryos: duck (embrio duck — ED), and later chick

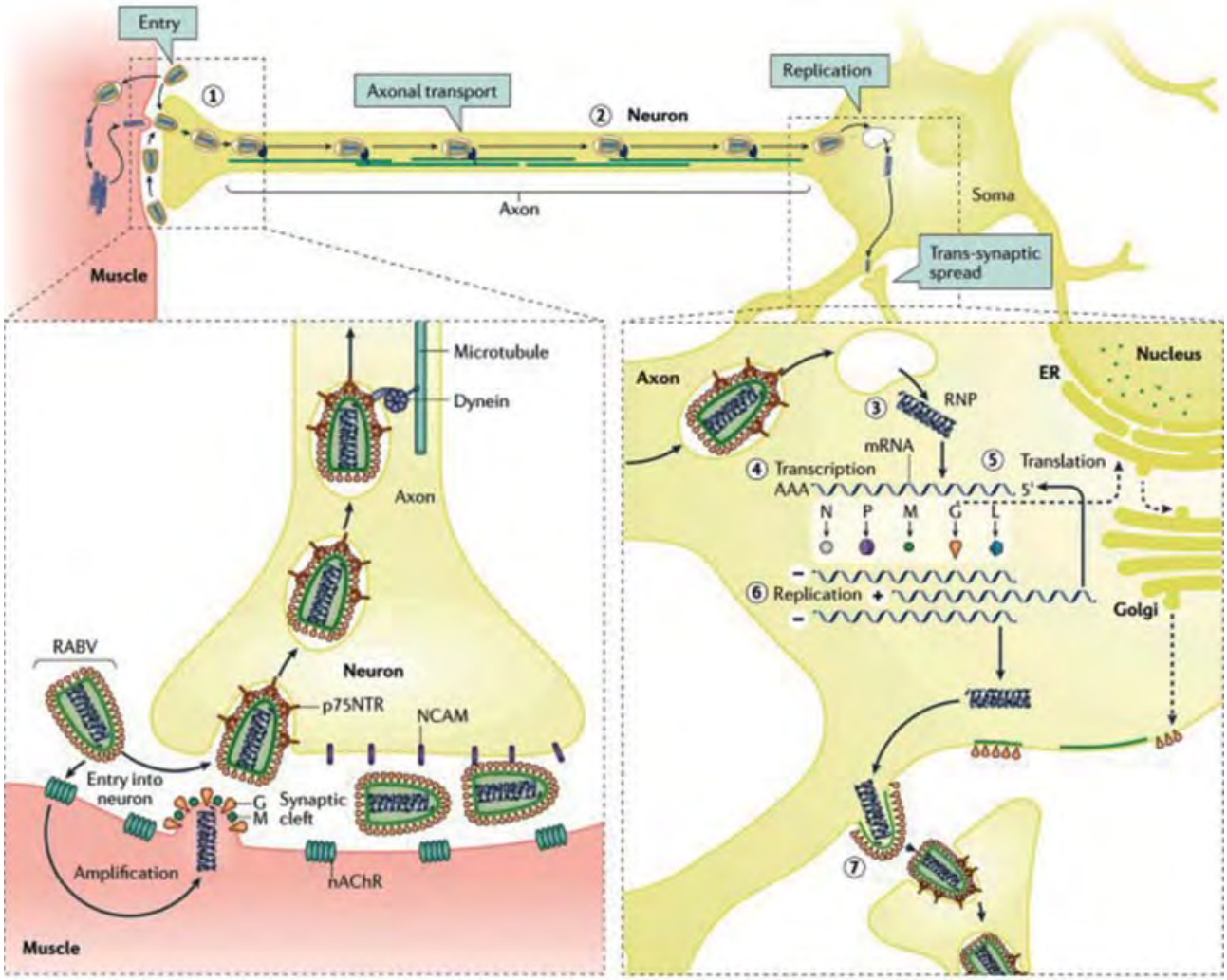

Fig. 2. **Diagram of RV penetration into the nervous system [5]:**
1 — receptor-mediated RV endocytosis on the presynaptic membrane; *2* — retrograde axonal RV transport toward the neuron body; *3* — the ribonucleoprotein release from the endocytic vesicle; *4* — viral mRNA transcription; *5* — viral proteins translation; *6* — full-length RNA genomes replication; *7* — viral particles assembly and release from a cell

(embrio chick — EC) for RV cultivation. Cell culture-based Vacs contain RV that multiply in cell substrates. In the process of developing Vacs containing inactivated RV, it was proposed to use other cells: primary culture of hamster kidney cells, human diploid cells (HDC), Vero cells, etc. [10]. Simultaneously with these studies, the possibility of various RV strains application was studied (Table 1). Human studies of Vacs containing the RV Flury low egg passage (Flury-LEP) strain have shown no side effects. However, these Vacs were characterized by insufficient immunogenicity. The use of the RV Flury high egg passage (Flury-HEP) strain increased the Vacs immunogenicity compared to the Flury-LEP-based preparation, but was slightly lower than the brain vaccine. Vac with inactivated Flury virus grown on ED was more effective, but its immunogenicity was lower than the brain vaccines.

Further studies were carried out using a culture of human fetal fibroblasts, which were HDCs with a limited lifespan. It was soon shown that fetal fibroblasts were susceptible to human viruses and free of latent viruses [11]. By the early 1960s, the highly immunogenic HDC line was used for RV propagation. HDC Vacs were first licensed in Europe in 1976 and in the USA in 1980 and are still in use today. In 1985, a purified concentrated Vac against rabies was obtained on Vero cells, which has a high immunogenicity comparable to Vac on HDC [12–15].

Currently, the requirements for AntiRab-Vacs developed by WHO are presented in a series of technical reports published in different

years, in which the requirements for AntiRab-Vacs are constantly increasing [16–18]. The reports provide the basic requirements for the production and control of AntiRab-Vacs for humans. The document describes in detail the cell cultures and requirements for them, considers the RVs allowed for use to obtain AntiRab-Vacs and for their control. The used standards and the main provisions of the production technology are described: cultivation, purification, and inactivation (β-propiolactone, formalin, etc.), adjuvants (aluminum hydroxide), requirements for the vaccine at different production stages.

Over the past period, antiRab-Vacs obtained by growing RVs on ED have been developed. However, these Vacs are less immunogenic than Vac from brain tissue. For ED drugs, 14 to 23 daily vaccinations are recommended, but sometimes even such high doses do not protect against Rab after intense contact with the source of infection. Another disadvantage of these Vacs is that the Vacs also contained myelin proteins, which caused adverse reactions, and as a result, the drug was forbidden by the WHO.

Subsequently, antiRab-Vac was obtained in cell and tissue culture. Vacs prepared in cell culture were not only safer compared to the vaccines based on brain tissue due to the neurotropic tissue absence, but also more effective.

Then AntiRab-Vacs were obtained: purified duck embryonic vaccine (PDEV); HDC-based one; purified EC cells-based Vac; purified VERO cells-based AntiRab-Vac; adsorbed AntiRab-Vac (RVA) obtained from hamster kidney primary cell culture.

The technological process leading to the development of the above Vacs included: Pitman Moore RV strain adaptation to stable cell lines such as VERO cells (Abhayrab and Verorab); HDC MRC-5. HDC-based Vac is considered the gold standard drug.

Currently, various RV strains and cell cultures are used to obtain AntiRab-Vacs (Table 1).

Currently, Vacs obtained from various RV strains using cell cultures of various origin are used for the prevention of Rab in humans (Table 2).

Currently, antiRab-Vacs such as Rabavert and Rabipur, represented by inactivated RVs, are widely used. Since inactivated Vacs cannot induce strong immunity to provide long-term protection against RV infection, recipients must receive multiple vaccinations over time, which requires new technological approaches to create Vacs. Rabipur (Table 2) was the first purified Vac obtained from chick embryo cells was licensed in Germany in 1984 and then in 60 more countries. The immunogenicity of Vac Rabipur has been confirmed in numerous clinical trials [19].

Rabipur is produced using the Flury-LEP RV strain grown on a primary fibroblast culture of chicken embryo cells. Virus in Vac is inactivated with β-propiolactone and purified by continuous density gradient centrifugation. As a result, a highly concentrated preparation stabilized with polygenin is obtained, followed by lyophilization. Rabipur is produced in Marburg, Germany and Ankleshwar, India.

Below it is a technological scheme of AntiRab-Vac obtained through the use of RV Pitman Moore and a cell culture of chicken fibroblasts [20]:

1 — preparation of ED and EC according to the classical scheme (9–11 days, at a temperature of 35–37 °C and humidity of 70–90%, trypsinization and centrifugation);

2 — infection of the primary culture of ED RV fibroblasts — 7 passages (adaptation), after which the resulting strain was cultured on the EC fibroblast culture — 4 passages, the selected embryos were trypsinized, centrifuged and the cells were suspended in the growth medium to a final concentration of 1.7×10^6 cells/ml;

3 — the suspension of trypsinized cells was filtered through a nylon filter and centrifuged (1000–1500 rpm, 15 min, at 2–4 °C). The cell sediment was suspended in fresh growth medium,

Table 1. **Cell cultures and RV strains used to obtain AntiRab-Vacs for humans**

Cell culture type	RV strains
HDC — human diploid cell culture	Flury-LEP — 40–50 passages
Primary canine kidney cell culture	Flury-HEP — 227–330 passages
Vero — kidney epithelium cells of the green African monkey	Pitman moore
	Vnukovo 32
BNK 21 — neonatal hamster kidney culture	Paris Pasteur
Chicken embryo primary culture	Rabbit fix
Hamster kidney primary cell culture	Street –Alabama Duffering
Chicken embryo primary cell culture	Challenge Virus Standart (CVS) 111

Table 2. **Characteristics of inactivated AntiRab-Vacs for humans**

Name of the vaccines	Strain	Cell culture	Purification type	Inactivator	Excipients per dose	Manufacturer
Rabipur, liof. > 2,5 ME	Flury LEP	Chicken embryo fibroblasts	Zonal ultracentrifugation in a sucrose density gradient	β-propiolactone	Sucrose — 75 mg, Hydrolyzed Gelatin — 10 mg (Polygelin)	Chiron Behring vaccines, India
Verorab, liof. > 2,5 ME	Wistar Rabies PM W 138-1503-34	Vero	Zonal ultracentrifugation in a sucrose density gradient	β-propiolactone	Maltose — 26.3 mg HSA — 2.5 mg	Sanofi Pasteur, France
Indirab, liof. > 2,5 ME	PM	Vero	Chromatography, ultrafiltration	β-propiolactone	Maltose — 25.0 mg HSA — 5 mg Merthiolate — 0,01%	Bharat Biotech, India
Kokav, liof. > 2.5 ME	Vnukovo 32	Syrian hamster kidney cells	Ultrafiltration	UV irradiation	HSA — 10 mg, sucrose — 75 mg, hydrolyzed gelatin — 10 mg (polygelin)	Scientific Production Association NPO Microgen, Russia
Imovax rabies, liof. > 2,5 ME	Wistar Rabies PM W 138-1503-3M	HDC	Ultrafiltration	β-propiolactone	HSA — 100 mg, neomycin — 150 mcg	Sanofi Pasteur, France
RabAvert, liof. > 2,5 ME	Fix virus, LEP Flury	Chicken fibroblasts	Zonal ultracentrifugation in a sucrose density gradient	β-propiolactone	HSA — 0.3 mg, Na-EDTA — 0.3 mg, sodium glutamine – 1 mg, hydrolyzed gelatin —– 12 mg (polygelin)	Glaxo Smith Kline, Belgium

Note: * PM – RV Pitman Moore strain; Vero —the kidneys epithelium cells of the green African monkey; Polygelin — a polymer of urea and polypeptides from denatured bovine gelatin; HSA — human serum albumin.

mixed and re-centrifuged under the same conditions. The cell suspension was stirred for 5–10 min at 35 ± 2 °C. The final cell concentration was adjusted with the growth medium to a concentration of $1.4–2.2\times10^6$ cells/ml;

4 — the cell suspension was inoculated with RV and incubated (90–120 min at 35 ± 2 °C) with stirring to adsorb the virus on the cells. An RV-infected cell suspension with a virus was incubated at a temperature of 34.5 ± 0.5 °C for 6 days;

5 — on the 4^{th}–5^{th} day of cultivation, the supernatant was taken (the 1^{st} harvest) and fresh growth medium was added. On the 7^{th}–8^{th} day the 2^{nd} harvest was taken. The harvests were stored at 2–8 °C;

6 — virus harvests were united, purified and concentrated using sucrose density gradient ultracentrifugation in a zonal centrifuge at 35,000 rpm. Corresponding bands containing live RV were selected at a sucrose concentration of 35–40%. During the monitoring period, the RV concentrate was stored at minus 60 °C (sterility, endotoxins, immunogenicity, etc. were monitored);

7 — the concentrate was thawed at 37 °C and cooled at 4 ± 2 °C, diluted with a stabilizing solution (sucrose, hydrolyzed gelatin, human serum albumin, sodium salts) to an antigen content of 8.5 IU/ml. The pH in Vac was adjusted to 8 ± 1 with 10% NaOH;

8 — β-propiolactone was added to the viral suspension to a final concentration of 0.025%. Incubation was carried out at 2–6 °C and constant stirring for at least 48 hours until complete RV inactivation;

9 — filling of primary packaging, lyophilization and sealing;

10 — Vac control.

Currently research is ongoing to create new forms of AntiRab-Vac. Research is carried out in a number of directions (Fig. 3):

Live attenuated Vacs — LAV. Unlike inactivated Vacs, LAVs mimic natural

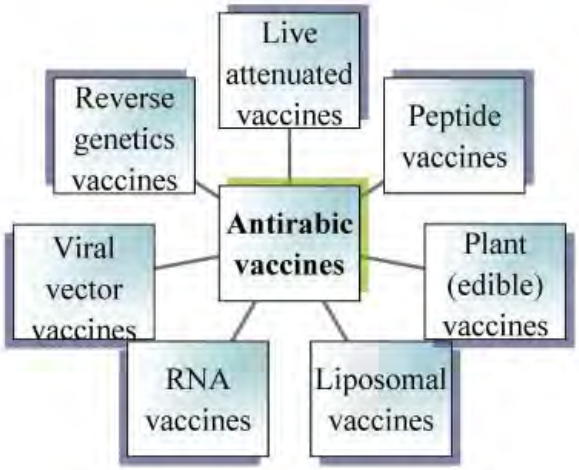

Fig. 3. **Types of vaccines against RV**

infection and often a single dose is sufficient to induce a sustained immune response. Until now, despite the wider use of LAV for oral vaccination against wild animals R (foxes, raccoons, etc.), LAV against domestic animals and humans R is still lacking. All LAVs used for wild animals are obtained as a result of repeated passage of SAD (street Alabama Dufferin) strains in cell culture, therefore, their possible return to virulence might become a practical limitation for their further development and usage for immunization of domestic animals, and especially for humans [21].

Peptide Vacs. There are known the works on the peptide Vacs creation against R. The effectiveness of the protein subunit, purified from the infected cells, G-protein for protection against R is studied. The G-protein of the R virus is the main protective antigen responsible for protective immunity against RV. In the study, the G-RV protein was introduced into a yeast cell and the resulting recombinant cell extracts containing the RV protein G protected guinea pigs from lethal RV infection when injected intramuscularly. However, these extracts did not protect mice infected with RV intracerebrally [22]. In general, Vacs based on RV protein subunits are low immunogenic and can cause limited immune responses.

AntiRab-Vacs of plant origin are the preparations based on transgenic plants, into the genome of which the corresponding fragment of the pathogenic microorganism genome has been inserted. In the literature, there are studies on the use of corn and tobacco for the RV G-protein expression for the production of "edible" Vac [23, 24]. Plant Vacs have not yet found application, despite the fact that the issue of creating such Vacs against RV and other infections has been studying for many years [25].

Liposomal (Ls) AntiRab-Vacs (LipoRV). LipoRV has been shown to promote the production of neutralizing antibodies to RV in BALBc mice. The Ls emulsion was prepared from hydrogenated soybean phosphatidylcholine and cholesterol. LipoRV consists of an Ls emulsion and an inactivated RV-Vac against RV. The immune response was compared between mice treated with LipoRV and inactivated AntiRab-Vac. In mice immunized with LipoRV, higher titers of the interleukin-2, interferon-gamma and the corresponding killer cells activity level were observed than in mice immunized with inactivated AntiRab-Vac. The authors' data also showed a higher survival value for mice that received 3 injections of LipoRV (56.2%) than 5 injections of inactivated AntiRab-Vac (40.6%) [26].

AntiRab-Vacs based on RNA. In the last decade, one of the strategies in the fight against infectious diseases has been RNA-Vac vaccination. Unlike DNA Vacs, which have a potential risk of integration with the host genome, RNA-based Vacs eliminate this danger. In addition, DNA-Vacs must be delivered to the nucleus and transcribed within the nucleus for antigen expression, which may not be effective in some cells. On the contrary, RNA-Vacs are directly translated into the cytoplasm, which not only eliminates the need for delivery to the nucleus, but leads to rapid antigen expression [27, 28]. RNA-based Vacs

are highly immunogenic and lead to consistent results [29, 30]. The impetus for the AntiRab-RNA-Vacs development could be the successful RNA-Vacs use for the COVID-19 prevention: RNA-Vacs of Pfaizer and Moderna firms. For example, Pfaizer Vac is a nucleoid-modified mRNA encoding a mutant form of the SARS-COV-2 spike protein, which is encapsulated in biodegradable lipid nanoparticles.

AntiRab-Vac based on viral vectors. Currently, a number of AntiRab-Vacs based on known viruses have been proposed: vesicular stomatitis, parainfluenza type 5, Newcastle disease, smallpox, human adenoviruses, etc. Genetically engineered vaccines based on these viral vectors make it possible to deliver into human or animal cells only genes encoding synthesis of the necessary antigens, which makes it possible not to use live pathogenic viruses when obtaining Vac. Recombinant Vacs are widely used today to control R in wild carnivores. A smallpox vaccine virus clone has been isolated, which forms the surface glycoprotein (G) RV. Vac containing recombinant cowpox virus carrying the gene for the basic glycoprotein (G) of the RV envelope has been obtained. Vac is often used orally to immunize foxes. Vac based on canine adenovirus has been created [31].

Vac against R obtained using reverse genetics method. Reverse genetics can reveal the function of genes. The researchers manipulate the genes sequence, changing or turning off a particular gene, and analyze what changes this leads to. This is the path of reverse genetics: from gene to trait, it has made it possible to create a new generation of AntiRab-Vacs [32, 33]. Reverse genetic methods offer an alternative solution for the development of safe and effective LAVs to prevent R, for example, the amino acid at position 333 of the glycoprotein (G) in several fixed RV strains is responsible for pathogenicity in adult mice. It was found that arginine at position 333 promotes the reversal of pathogenicity. In [21], a replicon was proposed as a live weakened AntiRab-Vac, in which the structural genes of Venezuelan equine encephalitis (VEEV) were replaced with the RV-G glycoprotein. Plasmid VEEV-RV-G was constructed using standard recombinant DNA techniques. The resulting glycoprotein sequence was amplified using an infectious clone as template and cloned into the VEEV replicon expression vector of alpha virus at AscI and PacI sites.

To further characterize VEEV-RV-G, the VEEV-RV-G particles were purified by ultracentrifugation and the protein composition of these particles was analyzed by SDS-PAGE. The RV-G protein was the only RV structural protein found in viral particles.

Bulky spherical particles of about 60–90 nm were observed on the surface of cells infected with VEEV-RV-G compared to the typical bullet-shaped RV particles. It has been shown that VEEV-RV-G can collect infectious viral particles that are very different from RV in both shape and size.

Glycoprotein-G (RV) provides efficient packaging of replicon chimeric RNA into infectious particles that can self-propagate in cell culture at high titers. VEEV-RV-G particles were highly attenuated in suckling mice and could induce strong humoral immune responses at relatively low doses. The mice were vaccinated with VEEV-RV-G intramuscularly, which protected the animals from lethal outcome in case of intracerebral infection with RV — CVS-24.

A number of studies and review materials are devoted to the creation, study and use of AntiRab-Vacs. The effectiveness of existing AntiRab-Vacs and the prospects for their development have been discussed in recent years [1, 19, 32, 34–36].

During the development and manufacture of Vacs, it is important to maintain the stability of the strains used. The development of molecular biology and biotechnology makes it possible to confirm the RV strains authenticity and their stability. The analysis of the Vnukovo-32 strain used to obtain AntiRab-Vac (cultured purified inactivated dry (KOKAV, Russia)) was performed. It was shown that the RNA structure of Vnukovo-312, CVS RV strains, which encodes a part of the G protein fragment, corresponds to a similar RNA fragment of RV. The 539 bp RNA structure of the RV strain, which encodes a fragment of protein G, is stable at all technology stages. The possibility of using restriction analysis to confirm the authenticity of the Vnukovo-32 RV strain at all stages of production, including the finished Vac form, has been shown [37].

Conclusions

Currently, inactivated viral Vacs are widely used for prevention of a number of infections. Some inactivated viral Vacs have been in use for decades and are generally well tolerated. Since viruses, when grown *in vitro*, usually enter the cell culture medium, they are separated from the infected cultures. The large viral particle size in comparison

with other macromolecules in the medium enables for easy particles separation using simple purification technologies based on separation of particles by size. The examples of such vaccines include polio virus, influenza virus, RV, and Japanese encephalitis virus. In an alternative approach used in the case of a killed viral vaccine (hepatitis A (HAV), Covid), the infected cells are lysed and the viral particles are purified. Viral particles are chemically inactivated, usually by treatment (β-propiolactone, formalin, radiation), and then the effect of the inactivated virus can be enhanced by adjuvants (for example, aluminum hydroxide or aluminum phosphate). It is possible to use Ls [25, 34] to enhance the immunogenicity of viral Vacs. Inactivated viral Vacs usually have high immunological activity, for example, 1 dose of hepatitis A vaccine provides protection in an amount of 50 ng. Thus, this classic strategy, characterized by an impeccable history of well-tolerated and effective vaccines creation, remains a very promising technology of choice for many viral Vacs, including AntiRab-Vacs.

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БІОТЕХНОЛОГІЧНІ ДОСЛІДЖЕННЯ ПРИ СТВОРЕННІ ТА У ВИРОБНИЦТВІ АНТИРАБІЧНИХ ВАКЦИН

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Сказ — неврологічне захворювання вірусного походження, що призводить до летальних наслідків. Вірус сказу є РНК-вірусом, який, проникаючи у центральну нервову систему, спричинює дисфункцію нейронів. Своєчасна вакцинація дає змогу запобігти розвиткові захворювання.

Мета. Статтю присвячено імунобіотехнологічним дослідженням, спрямованим на створення антирабічних вакцин.

Результати. Розглянуто історію створення таких вакцин – від перших інактивованих, отриманих з нервової тканини, до вирощування вірусу на культурах клітин тварин. Наведено дані про наявні на ринку антирабічні вакцини: їхній склад, використовувані штами вірусу сказу, культури клітин, способи інактивації та очищення вірусу. Описано технологію отримання антирабічної вакцини на основі штаму вірусу Pitman Moore і культури клітин курячих фібробластів. Розглянуто переваги різних видів вакцин: живих атенуйованих, пептидних, ліпосомальних, РНК-вакцин, вакцин, отриманих на основі вірусних векторів, трансгенних рослин і методів зворотної генетики.

Висновки. Розвиток біотехнології, імунології та вірусології дає змогу постійно вдосконалювати вакцинні препарати, зокрема й проти сказу, підвищуючи їхню ефективність і безпеку.

Ключові слова: імунобіотехнологія; вірусні вакцини; антирабічна вакцина; РНК-вірус; вірус сказу.

БИОТЕХНОЛОГИЧЕСКИЕ ИССЛЕДОВАНИЯ ПРИ СОЗДАНИИ И В ПРОИЗВОДСТВЕ АНТИРАБИЧЕСКИХ ВАКЦИН

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Бешенство — неврологическое заболевание вирусной природы, приводящее к летальному исходу. Вирус бешенства представляет собой РНК-вирус, который, проникая в центральную нервную систему, приводит к дисфункции нейронов. Своевременная вакцинация позволяет предотвратить развитие заболевания.

Цель. Статья посвящена иммунобиотехнологическим исследованиям, направленным на создание антирабических вакцин.

Результаты. Рассмотрена история создания антирабических вакцин – от первых инактивированных, полученных из нервной ткани, до выращивания вируса на культурах клеток животных. Приведены данные об имеющихся на рынке антирабических вакцинах: их составе, используемых штаммах вируса бешенства, культурах клеток, способах инактивации и очистки. Описана технология получения антирабической вакцины на основе штамма вируса Pitman Moore и культуры клеток куриных фибробластов. Рассмотрены преимущества разных видов вакцин: живых аттенуированных, пептидных, липосомальных, РНК-вакцин, вакцин, полученных на основе вирусных векторов, трансгенных растений и методов обратной генетики.

Выводы. Развитие биотехнологии, иммунологии и вирусологии позволяет постоянно совершенствовать вакцинные препараты, в том числе и против бешенства, повышая их эффективность и безопасность.

Ключевые слова: иммунобиотехнология; вирусные вакцины; антирабическая вакцина; РНК-вирус; вирус бешенства.