РОЗДІЛ ІІІ. ФІЗІОЛОГІЯ ЛЮДИНИ ТА ТВАРИН

UDC 578.835:615.37

CURRENT STATE AND FUTURE TRENDS IN DEVELOPMENT AND PRODUCTION OF POLIOMYELITIC VACCINES

Galkin O.Yu., Metalnikova N.P., Gorgo Yu.P.

National Technical University of Ukraine "Kyiv Polytechnic Institute"
03056, Ukraine, Kyiv, Peremogy av., 37

alexfbt@mail.ua

The literary data concerning the history of creation, manufacture and characteristics of polio vaccines are summarized in the review of the literature. The prerequisites of their creation are examined. The resume about advantages and disadvantages of existing vaccines are made. Optimal immunization scheme is described. The perspective of creation of a new vaccine using the recombinant technologies is examined.

Key words: poliomyelitis, live, inactivated, recombinant polio vaccine, combined immunization scheme.

СУЧАСНИЙ ПІДХІД ТА ПЕРСПЕКТИВИ РОЗРОБКИ Й ОТРИМАННЯ ПОЛІОМІЄЛІТНИХ ВАКЦИН

Галкін О.Ю., Метальнікова Н.П., Горго Ю.П.

Національний технічний університет України «Київський політехнічний інститут»
03056, Україна, Київ, пр. Перемоги, 37

alexfbt@mail.ua

У літературному огляді узагальнені літературні дані щодо історії створення, виробництва та характеристик поліомієлітних вакцин, розглянуті передумови їх створення. Зроблені висновки щодо переваг та недоліків вакцин, які використовуються на даний момент. Розглянута перспектива створення нової вакцини з використанням рекомбінантних технологій.

Ключові слова: поліомієліт, жива, інактивована, рекомбінантна поліомієлітна вакцина, комбінована схема імунізації.

СОВРЕМЕННЫЙ ПОДХОД И ПЕРСПЕКТИВЫ РАЗРАБОТКИ И ПОЛУЧЕНИЯ ПОЛИОМИЕЛИТНЫХ ВАКЦИН

Галкин А.Ю., Метальникова Н.П., Горго Ю.П.

Национальный технический университет Украины «Киевский политехнический институт»
03056, Украина, Киев, пр. Победы, 37

alexfbt@mail.ua

В обзоре литературы обобщены литературные данные об истории создания, производстве и характеристиках полиомиелитных вакцин, рассмотрены предпосылки их создания. Сделаны выводы о преимуществах и недостатках вакцин, которые используются в данный момент. Описана оптимальная схема иммунизации. Рассмотрена перспектива создания новой вакцины с использованием рекомбинантных технологий.

Ключевые слова: полиомиелит, живая, инактивированная, рекомбинантная полиомиелитная вакцина, комбинированная схема иммунизации.

INTRODUCTION

Poliomyelitis is a widespread disease, which has been studied for a long time. Since effective methods for treatment hadn't been found, the investigations for making a vaccine were started. Developments were conducted in several lines and aren't finished until now. Different vaccines and vaccination schemes exist and each of them has their own advantages and disadvantages. That's why it is necessary to summarize existing information about vaccines and their manufacture, side effects, latest elaborations, etc. The purposes of this article are: to analyse literature sources about modern elaborations in making poliomyelitic vaccines, examine the history of creation of vaccines, summarize data about biotechnological bases of manufacture of vaccines, and make a resume about optimal, for the present time, vaccination scheme.

The aim of our work was to analyze the contemporary literature data schodopidhodiv to the development and production of polio vaccine and identifying promising directions in this area.

CREATION OF POLIO VACCINES: HISTORY AND PRECONDITIONS

Poliomyelitis is a disease of great antiquity. By the mid-19th century, the Industrial Revolution had brought increased urbanization to Europe and North America and, with it, significant changes and improvements in living conditions. Coincident with these massive changes was the advent of larger and more frequent outbreaks of poliomyelitis. From the late 1800s, outbreaks were occurring in several European countries and in the United States, and they remained a dominant public health problem in the developed world for the first half of the 20th century. There is no treatment for polio, outside of easing of symptoms, that's why necessity of creation a polio vaccine was evident. A major landmark in the study of poliomyelitis was the successful passage of the virus to nonhuman primates by Landsteiner and Popper in 1909. This advance, and the recognition of three distinct serotypes, opened the way for all subsequent work on vaccines and study of the biochemical and biophysical properties of the polioviruses [1-3].

By the 1950s, two different approaches to the prevention of poliomyelitis by vaccination were developed. In 1954 Salk and Younger produced the first successful polio vaccine – inactivated polio vaccine (IPV). This vaccine is produced in the following way: viruses are grown in suspension cell culture for certain time, then cell biomass is destroyed by freezing and thawing method. After that suspension viruses are separated and chemically inactivated using formaldehyde. Suspension is purified and concentrated by ultrafiltration and after quality control it is used as a vaccine. For propagating viruses the transferred cell lines, such as HeLa, Hep-2, Girardi Heart, HT-1080, are used.

CHARACTERISTICS OF INACTIVATED POLIO VACCINE

IPV is completely non-infectious, yet, following injection, it elicits an immune response that is protective against paralytic disease. IPV cannot cause poliomyelitis and thus is safe for use in immunocompromised persons and their contacts [4, 5, 6]. IPV produces protective antibodies in the blood (serum immunity). This serum immunity prevents the spread of the virus to the central nervous system and provides protection against polio paralysis. The suggested immunity is prolonged and perhaps lifelong: circulating antibodies have persisted for at least 10 years. However, IPV induces only low levels of immunity (via secretary IgA) to poliovirus in the gut. The Salk vaccine is given in two intramuscular injections spaced one month apart and requires boosters every 5 years [1, 5, 7].

In 1988 enhanced-potency IPV (eIPV) formulation became available; eIPV contains higher D-antigenic units per dose for types 2 and 3 than standard IPV. After 2 doses of enhanced-potency IPV, high levels of serum-neutralizing antibodies to all 3 types of poliovirus appears in 94-100% of individuals, and after 3 doses, seroconversion appears in 99-100% of individuals. Enhanced-potency IPV induces mucosal immunity by inhibiting pharyngeal acquisition of poliovirus and, to a lesser extent, intestinal acquisition, yet the extent of mucosal immunity induced by IPV is far less than oral polio vaccine [8].

Advantages of the IPV are: the virus is not live, thus it is easier to manage than oral polio vaccine; there is no risk of vaccine-associated paralytic poliomyelitis (VAPP); immunization triggers an excellent immune response and long-lasting immunity to all 3 poliovirus types; no serious adverse effects to date exist.

Disadvantages of the IPV are: 1) IPV induces only little immunity in intestinal tract: if an individual is infected with the wild-type poliovirus, the virus can multiply in the intestines and be shed in stools, ultimately heightening the risk of viral circulation within the community; 2) The price of IPV is over 5 times that of oral polio vaccine (OPV); 3) Administering of IPV requires trained health workers; 4) IPV requires additional injections in infants until new combination products are available [2, 4, 5, 9].

Widespread immunization with IPV has virtually eliminated poliomyelitis in most developed countries. In 1988, the World Health Organization set a goal of eradication of poliomyelitis from the entire world by the year 2000. In the context of the WHO Global Initiative, the number of cases of poliomyelitis has decreased by 99% [10].

CHARACTERISTICS OF ORAL POLIO VACCINE

During the same period, many laboratories sought to produce live, attenuated polio vaccines. The oral polio vaccine was developed in 1958 by Albert Sabin. Sabin attenuated the wild type poliovirus by passaging the virus in monkey kidney epithelial cells [2]. Now OPV is produced in the same way with IPV only without chemical inactivation, because virus strains are non-infectious. The commonly used form of the oral polio vaccine is trivalent, which means that it contains live attenuated strains of the three serotypes of poliovirus. Trivalent OPV is characterized in vivo by efficient growth properties in the intestinal tract, unaltered immunogenic properties with respect to wild type progenitors, and attenuated neurovirulence after experimental intraspinal injection into primates. This means that an individual immunized with trivalent OPV induces long-lasting (frequently life-long) protective immunity of the gastrointestinal tract to all known forms of poliovirus [3, 9].

The Sabin oral vaccine is given in 3 doses in the first two years of life, and a booster is given when the child starts school [7, 11]. Since the three attenuated strains of poliovirus present in the OPV interfere with each other's replication in the intestine, boosters of OPV are required to induce protective immunity to all three polio serotypes. In the first immunization, one strain will grow most effectively, and immunity to this strain will be induced. With the second immunization, the immune response generated to the first strain will inhibit the growth of that same strain, such that a second strain will replicate most successfully, inducing immunity to the second strain. Similarly, immunity is induced to the third strain with the third booster [6, 9]. Further boosters are not given unless the patient is exposed to polio or will be travelling to an endemic region [1].

In the opinion of many, the OPV is nearly ideal for use in polio eradication [12-14]. Since attenuated vaccines are capable of transient growth, the OPV allows prolonged exposure of the immune system to the epitopes on the attenuated organisms, resulting in increased immunogenicity and memory-cell development. It is easily administered by mouth, facilitating its widespread use; it induces intestinal immunity, making recent OPV recipients resistant to infection by wild polioviruses and effectively blocking wild poliovirus transmission when used in mass campaigns; and it provides long-term protection against polio through durable humoral immunity. OPV virus can spread to and immunize unvaccinated contacts of vaccine recipients, increasing the impact of OPV beyond those actually immunized. Through effective use of this excellent vaccine, the WHO Global Polio Eradication Initiative has nearly achieved its goal of eradicating wild polioviruses [15, 16].

OPV cannot be used for patients with compromised immune systems because it is a live virus and can cause disease in these patients. It also cannot be used by those in close contact with immunocompromised patients because the live virus in the vaccine can be shed in the faces of those who ingest it, and can possibly be transmitted to the immunocompromised patient [1, 12]. Another disadvantage of the Sabin oral vaccine is that those who have an enterovirus infection of the gastrointestinal tract when taking the oral vaccine may not develop the immune response [2].

The monovalent oral polio vaccine 1 or mOPV1, is currently used in Egypt as a critical part of a new WHO strategy to end polio type 1 transmission (types 2 and 3 polioviruses have already been eliminated from Egypt). The production of mOPV was based on existing trivalent OPV but with appropriate “change control” procedures to assure the quality of the product, and to distinguish mOPV from trivalent OPV [17, 18].

VACCINE-ASSOCIATED PARALYTIC POLIOMYELITIS AND PROBLEM OF CIRCULATION OF VACCINE-DERIVED POLIOVIRUSES

The main disadvantage of OPV is the possibility of VAPP, which can occur when oral polioviruses revert to a more virulent form. In fact, in any attenuated vaccine, there exists a danger that the attenuated form will revert to the virulent form. The much higher incidence of polio from wild poliovirus infections at the time, however, mitigated concern over the rare occurrence of VAPP, and it has only been in recent years that VAPP has become an increasingly significant proportion of the global polio burden [12, 19]. Occasionally, immunodeficient persons exposed to OPV become chronically infected [20-22], excreting derivatives of the OPV strains for many months or years [12, 23-25]. Chronic OPV excerptors, however, seem to be very rare, and have so far been found only in upper- and middle-income countries where appropriate clinical management of immunodeficiency is available [26].

In retrospect, it is remarkable that OPV has attained such an outstanding record of safety and efficacy over the four decades of worldwide use [14, 19]. It is now known that most RNA viruses have highly mutable genomes that are potentially capable of very rapid evolution, many orders of magnitude faster than the genomes of DNA viruses or cellular organisms [27, 28], and polioviruses are among the most rapidly evolving of all RNA viruses [12, 23-25, 29, 30]. Moreover, the attenuating mutations of the OPV strains are strongly selected against when the vaccine replicates in the intestinal tract of OPV recipients [31-33]. To counter the daunting challenges of delivering a live, attenuated RNA virus vaccine via its natural route of infection, immunization strategies were developed to minimize adverse events [12, 34]. In developed countries, OPV was first delivered in mass campaigns to achieve high rates of coverage, and this was followed by a strategy of comprehensive routine immunization. Similar strategies were adopted in developing countries, with mass OPV campaigns often playing a more prominent role than routine immunization. In most instances, OPV was delivered in the context of pre-existing high population immunity to poliovirus, because of recent exposure to circulating wild polioviruses or, as with developed countries in the early 1960s, from the combination of immunity acquired from natural infection and immunity acquired from several years of immunization with the inactivated poliovirus vaccine (IPV). These strategies probably minimized the epidemiological consequences of the frequent phenotypic reversion of the OPV strains [11, 35].

While reversion to nearly wild-type phenotype regularly occurs soon after the onset of OPV reproduction in the gastro-intestinal tract of vaccine recipients or their contacts, this is usually not a big problem, provided the vaccine is used either for mass vaccination or in populations with a relatively high level of anti-polio immunity. However, if these conditions are not met, the vaccine viruses are likely to be converted into highly transmissible agents with a nearly wild-type level of neurovirulence [36]. Moreover, OPV viruses may persist and evolve even in adequately immunized populations. The current strategy for the "endgame" of poliovirus eradication envisions cessation of OPV usage shortly after the last isolation of a wild poliovirus [16, 17, 35]. If implemented, this strategy would result in rapid growth of non-immune human populations at the time when OPV derivatives would very likely be persisting. Safe discontinuation of OPV vaccination will be possible only after an efficient new vaccine or an anti-poliovirus drug is available. To achieve this goal, stimulation of poliovirus research and elimination of organizational and financial obstacles preventing it are needed [11, 16, 37].

VAPP occurs more frequently after administration of the first dose of OPV in the all-OPV series than after subsequent doses; the risk of VAPP is one case per 750,000 doses distributed for the first dose of oral poliovirus vaccine (OPV) and one case per 2.4 million doses of OPV distributed overall. Because of this risk, vaccine schedule that starts with IPV is preferred, even though extra injections are required [38].

THE COMBINED SCHEME OF IMMUNIZATION

The American Academy of Family Physicians (AAFP) and the Advisory Committee on Immunization Practices (ACIP) now recommend that the first two doses of poliovirus vaccine should be IPV. OPV is no longer recommended for the first two doses and is acceptable only in special circumstances. The combined IPV/OPV schedule for routine immunization against poliomyelitis includes two doses of IPV administered at two and four months of age followed by two doses of OPV administered at 6 to 18 or 12 to 18 months of age and at four to six years of age [10, 39].

Most studies have shown that two doses of IPV induce protective levels of antibodies in 90 percent or more of recipients [40]. Thus, when OPV is administered as part of the sequential schedule, most recipients already have humoral seroprotection due to IPV, which should greatly reduce the incidence of VAPP occurring after the first dose of OPV.

The sequential immunization schedule provides better intestinal immunity than the all-IPV schedule [41]. The percentage of children who shed poliovirus in their stools after being given a challenge dose of OPV is 85 % after the administration of three doses of IPV; 66 % after the administration of two doses of IPV and one previous dose of OPV; 25 % after the administration of two doses of IPV and two previous doses of OPV; and 24 % after the administration of two doses of IPV and three previous doses of OPV. Based on this data, the ACIP concluded that two doses of OPV were necessary in the sequential schedule [40]. Priming with IPV in the sequential schedule does not reduce reversion of attenuated OPV viruses to virulent forms; thus, unvaccinated persons in contact with persons being immunized on the IPV/OPV sequential schedule still have a very small risk for VAPP; however, shedding of serotype 3 poliovirus may be reduced in vaccine recipients [10].

A NEW TREND: THE RECOMBINANT VACCINE

In the exciting research field of recombinant biotechnology, scientists are also attempting genetic alteration of the poliovirus. Researchers are using Escherichia coli as a host for bacterial gene cloning. Work is being done to take the genes of poliovirus, which code for the synthesis of the viral capsid (the protein coat of a virus particle) and to combine it with E.coli's genes. The E. coli can then synthesize viral capsid proteins to be used in making a vaccine. This latter approach eliminates any possibility of the virus infecting the vaccinated patient because the vaccine contains only a part of the virus, excluding potentially dangerous content.

DNA vaccines successfully elicit an immune response, although the mechanism of this response is as yet undetermined. A potential risk of using DNA vaccines in humans is that injecting naked DNA might not be safe; this foreign DNA could insert itself into and damage human chromosomes and potentially increase the risk of cancers or autoimmune disorders [42].

There are no effective methods for treatment of poliomyelitis. Vaccination is only effective way to control poliomyelitis and there is no doubt of its necessity. Existing vaccines – OPV and IPV – are nearly answered the demands and are used in combined immunization schedule. However, in connection with risk of VAPP and discomfort of multiple doses of vaccine investigations in the field of recombinant biotechnology are carried out. DNA vaccine, which only contains a part of virus and cannot cause the disease, has been developed.

Further research may focus on the analysis of modern technological approaches to obtaining polio vaccines (live, inactivated, and recombinant).

LITERATURE

1. Mensi C. Poliomyelitis: Present epidemiological situation and vaccination problems / C. Mensi, F. Pregliasco // Clin. Diagnostic Lab. Immunol. – 1998. – Vol. 5, № 3. – P. 278-280.

2. Poliomyelitis. In: Epidemiology and prevention of vaccine-preventable diseases. – Atlanta: National Immunization Program, 1998. – P. 249-262. – (Forth Edition).
3. Modlin J. Poliomyelitis and poliovirus immunization / In: Human Enterovirus Infections, Editor H.A. Rotbart. – Washington: ASM Press, 1995. – P. 195-220. – (First Edition).
4. Salk J. Are booster doses of poliovirus vaccine necessary? Jonas Salk proposes a scientific evaluation / J. Salk // Vaccine. – Vol. 8, № 5. – P. 419-420.
5. Murdin A.D. Inactivated poliovirus vaccine: past and present experience / A. D. Murdin, L. Barreto, S. Plotkin // Vaccine. – 1996. – Vol. 14. – P. 735-746.
6. Plotkin S. Current issues in the efficacy of oral poliovirus vaccine and inactivated poliovirus vaccine immunization / S. Plotkin // Pediatr. Infect. Dis. J. – 1997. – Vol. 10, № 12. – P. 979-981.
7. Faden H. Poliovirus vaccination / H. Faden // J. Infect. Dis. – 1993. – Vol. 28, № 8. – P. 25-28.
8. Duchene M. Production, testing and perspectives of IPV and IPV combination vaccines: GSK biologicals' view / M. Duchene // Biologicals. – 2006. – Vol. 34, № 2. – P. 163-166.
9. Beal A.J. Efficacy and safety of oral poliovirus vaccine and inactivated poliovirus vaccine / A.J. Beal // Pediatr. Infect. Dis. J. – 1991. – Vol. 10, № 12. – P. 970-972.
10. Mateen F.J. Oral and inactivated poliovirus vaccines in the newborn: A review / F.J. Mateen, R.T. Shinohara, R.W. Sutter // Vaccine. – 2013. – Vol. 31, № 21. – P. 2517-2524.
11. Oita I. Poliovirus separation from cell extracts using capillary electrophoresis: Potential use in vaccine production and control? / I. Oita, H. Halewyck, S. Pieters // J. Virol. Meth. – 2012. – Vol. 185, № 1. – P. 7-17.
12. Bonnet M.C. World wide experience with inactivated poliovirus vaccine / M.C. Bonnet, A. Dutta // Vaccine. – 2008. – Vol. 26, № 39. – P. 4978-4983.
13. Nathanson N. Poliomyelitis eradication – a dangerous endgame / N. Nathanson, P. Fine // Science. – 2002. – Vol. 296, № 5566. – P. 269-70.
14. Polio eradication: the OPV paradox / [Dowdle W.R., De Gourville E., Kew O.M. et al.] // Rev. Med. Virol. – 2003. – Vol. 13, № 5. – P. 277-291.
15. World Health Organization. Progress towards the global eradication of poliomyelitis // Weekly Epidemiological Record. – 2003. – Vol. 78. – P. 138-144.
16. Heymann D.L. Polio eradication: finishing the job and protecting the investment / D.L. Heymann // Bulletin of the World Health Organization. – 2004. – Vol. 82, №1. – P. 32-38.
17. Heymann D.L. A vision of a world without polio: The OPV cessation strategy / D.L. Heymann, Sutter R.W., Aylward R.B. // Biologicals. – 2006. – Vol. 34, № 2. – P. 75-79.
18. Graf H. Manufacturing and supply of monovalent oral polio vaccines / H. Graf // Biologicals. – 2006. – Vol. 34, № 2. – P. 141-144.
19. Fine P. Transmissibility and persistence of oral polio vaccine viruses: implications for the global poliomyelitis eradication initiative / P. Fine, I. Carneiro // American J. Epidemiol. – 1999. – Vol. 150, № 10. – P. 1001-1021.
20. Vaccine-associated poliomyelitis in a child with sex-linked agammaglobulinemia / [Wright P.F., Hatch M.H., Kasselberg A.G. et al.]// J. Pediatrics. – 1977. – Vol. 91, №3. – P. 408-412.
21. Sutter R.W. Vaccine-associated paralytic poliomyelitis among immunodeficient persons / R.W. Sutter, R. Prevots // Infections in Medicine. – 1994. – Vol. 11. – P. 426-438.
22. Persistence of vaccine-derived polioviruses among immunodeficient persons with vaccine-associated paralytic poliomyelitis / [Khetsuriani N., Prevots D.R., Quick L.et al.] // J. Infect. Diseases. – 2003. – Vol. 188, № 12. – P. 1845-1852.

23. Prolonged replication of a type 1 vaccine-derived poliovirus in an immunodeficient patient / [Kew O.M., Sutter R.W., Nottay B.K.et al.] // J. Clin. Microbiol. – 1998. – Vol. 36, № 10. – P. 2893-2899.
24. Evolution of poliovirus type I during 5.5 years of prolonged enteral replication in an immunodeficient patient / [Bellmunt A., May G., Zell R. et al.] // Virol. – 1999. – Vol. 265, № 2. – P. 178-184.
25. Evolution of the Sabin strain of type 3 poliovirus in an immunodeficient patient during the entire 637-day period of virus excretion / [Martin J., Dunn G., Hull R. et al.] // J. Virol. – 2000. – Vol. 74, № 7. – P. 3001-3010.
26. Search for poliovirus carriers among people with primary immune deficiency diseases in the United States, Mexico, Brazil, and the United Kingdom / [Halsey N.A., Pinto J., Espinosa-Rosales F.et al.] // Bulletin of the World Health Organization. – 2004. – Vol. 82, № 3. – P. 37-39.
27. Domingo E. RNA virus mutations and fitness for survival / E. Domingo, J. Holland // Ann. Rev. Microbiol. – 1997. – Vol. 51. – P. 151-178.
28. Drake J.W. Mutation rates among RNA viruses / J.W. Drake, J.J. Holland // Proceedings of the National Academy of Sciences of the United States of America. – 1999. – Vol. 96, № 24. – P. 13910-13913.
29. Evolution of circulating wild poliovirus and of vaccine-derived poliovirus in an immunodeficient patient: a unifying model / [Gavrilin G.V., Cherkasova E.A., Lipskaya G.Y. et al.] // J. Virol. – 2000. – Vol. 74, № 16. – P. 7381-7390.
30. Liu H.-M. Molecular evolution of a type 1 wild-vaccine poliovirus recombinant during widespread circulation in China / H.-M. Liu, D.P. Zheng, L.B. // J. Virol. – 2000. – Vol. 74, № 23. – P. 11153-11161.
31. Minor P.D. The effect of sequences in the 5' non-coding region on the replication of polioviruses in the human gut / P.D. Minor, G. Dunn // J. General Virol. – 1988. – Vol. 69, № 5. – P. 1091-1096.
32. Prevalence of vaccine-derived polioviruses in the environment / [Yoshida H., Horie H., Matsuura K.et al.] // J. General Virol. – 2002. – Vol. 83, № 5. – P. 1107-1111.
33. Minor P.D. Poliovirus vaccines: molecular biology and immune response. In: Molecular biology of picornaviruses / Minor P.D. [Editors B.L. Semler, E. Wimmer]. – Washington: ASM Press, 2002. – P. 381-390. – (First Edition).
34. Sabin A.B. Live, orally given poliovirus vaccine. Effects of rapid mass immunization on population under conditions of massive enteric infection with other viruses / A.B. Sabin, M. Ramos-Alvarez, J. Alvarez-Amezquita // J. American Med. Association. – 1960. – Vol. 173, № 14. – P. 1521-1526.
35. Smith J. Certification of polio eradication: process and lessons learned / J. Smith, R. Leke, A. Adams // Bulletin of the World Health Organization. – 2004. – Vol. 82, № 1. – P. 1-33.
36. Agol V.I. Vaccine-derived polioviruses / V.I. Agol // Biologicals. – 2006. – Vol. 34, № 2. – P. 103-108.
37. Nathanson N. From emergence to eradication: the epidemiology of poliomyelitis deconstructed / N. Nathanson, O.M. Kew // Am. J. Epidemiol. – 2010. – Vol. 172, № 11. – P. 1213-1229.
38. Ohka S. Recent insights into poliovirus pathogenesis / S. Ohka, A. Nomoto // Trends Microbiol. – 2001. – Vol. 9, № 10. – P. 501-506.

39. Mueller S. Poliovirus and poliomyelitis: A tale of guts, brains, and an accidental event / S. Mueller, E. Wimmer, J. Cello // Virus Research. – 2005. – Vol. 111, № 2. – P. 175-193.
40. Centers for Disease Control and Prevention. Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine; recommendations of the advisory committee on immunization practices (ACIP) // Morbid. Mortal. Weekly Rep. – 1997. – Vol. 46. – P. 1-25.
41. Antibody response and viral excretion after live polio vaccine or a combined schedule of live and inactivated polio vaccines / [Ramsay M.E., Begg N.T., Gandhi J. et al.] // Pediatr. Infect. Dis. J. – 1994. – Vol. 13, № 12. – P. 1117-1121.
42. Caldwell M. The Dream Vaccine / M. Caldwell // Discover. – 1997. – Vol. 9. – P. 3-5.

UDC 577.27:57.083.33

OBTAINING OF MONOCLONAL ANTIBODIES TO HUMAN IgG SUITABLE FOR USAGE IN HIGHLY SENSITIVE AND SPECIFIC IMMUNOASSAYS

[1,2]Galkin O.Yu., [3]Solovjova V.F., [1]Metalnikova N.P., [1]Dugan O.M., [1]Gorgo Yu.P.

[1]National Technical University of Ukraine "Kyiv Polytechnic Institute"
03056, Ukraine, Kyiv, Peremogy av., 37, [2]Hema Ltd.
03022, Ukraine, Kyiv, Vasilkovskaya str. 98
[3]Ukrainian Scientific & Research Institute of Nutrition, Biotechnology and Pharmacy
01042, Ukraine, Kyiv, Chygorina str., 18

alexfbt@mail.ua

The original set from 12 clones of hybridomas, producers of monoclonal antibodies (McAbs) against human IgG has been obtained. Criteria for selecting McAbs with satisfactory properties has been justified. Monoclonal antibodies with such properties have to provide high informativeness indexes (sensitivity and specificity) of immunoassay methods based on obtained McAbs. The study of following biological properties of McAbs has been conducted: specificity, constant of affinity and titer in a cultural medium. Obtained McAbs are directed to the two epitop regions on IgG molecule. The first group of McAbs relates to epitop region, represented by two epitopes; the second epitop region is represented by only one epitop.

Keywords: monoclonal antibodies, hybridomas, human IgG, affinity, epitop mapping.

ОТРИМАННЯ МОНОКЛОНАЛЬНИХ АНТИТІЛ ДО IgG ЛЮДИНИ, ПРИДАТНИХ ДЛЯ ВИКОРИСТАННЯ У ВИСОКОЧУТЛИВИХ І СПЕЦИФІЧНИХ МЕТОДАХ ІМУНОАНАЛІЗУ

[1,2]Галкін О.Ю., [3]Соловйова В.Ф., [1]Метальнікова Н.П., [1]Дуган О.М., [1]Горго Ю.П.

[1]Національний технічний університет України «Київський політехнічний інститут»
03056, Україна,Київ, пр. Перемоги, 37

[2]ТОВ «Хема»,
03022, Україна, Київ, вул. Васильківська, 98

[3]Український науково-дослідний інститут харчування, біотехнології та фармації
01042, Україна,Київ, вул. Чигоріна, 18

alexfbt@mail.ua

Одержано оригінальний набір з 12 клонів гібридом, продуцентів моноклональних антитіл (МкАт) до IgG людини. Проведено обґрунтування критеріїв відбору МкАт із властивостями, що забезпечуватимуть високі показники інформативності (чутливості та специфічності) розроблюваних на їх основі методів імуноаналізу. Проведено поглиблене вивчення таких біологічних властивостей антитіл: встановлено їхню специфічність, константу афінності та титр у культуральній рідині. Отримані антитіла спрямовані до двох епітопних регіонів на молекулі IgG.