НИИ ОЧБ

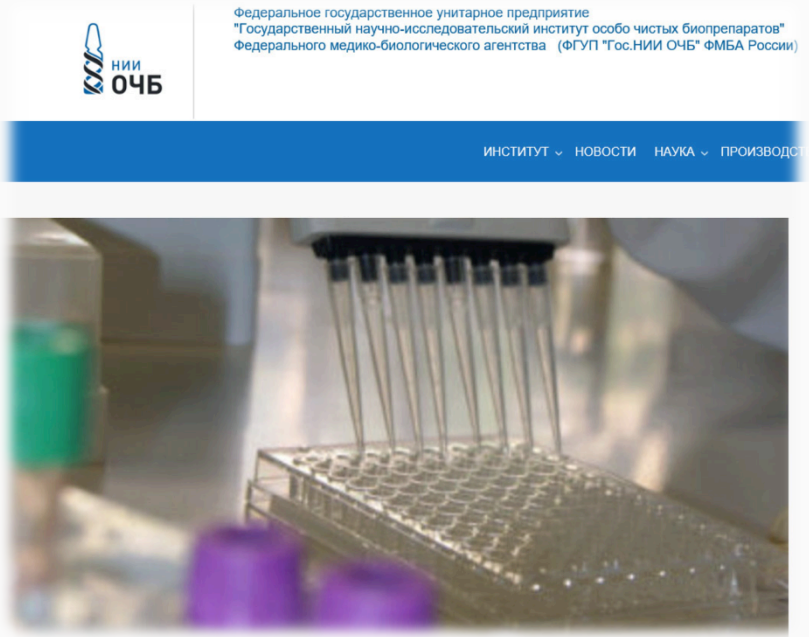
ПЕРСПЕКТИВЫ РАЗРАБОТКИ БИОПРЕПАРАТОВ И ИММУНОФАРМАКОЛОГИЧЕСКИХ СРЕДСТВ ДЛЯ ОБЕСПЕЧЕНИЯ ХИМИЧЕСКОЙ ЗАЩИТЫ И РЕПАРАЦИИ ПРИ РАДИАЦИОННЫХ ВОЗДЕЙСТВИЯХ

Ю.М. Васильев

ФГУП «Гос.НИИ ОЧБ» ФМБА России

secretary@hpb-spb.com

Конфликт интересов



- ФГУП «Гос.НИИ ОЧБ» ФМБА России является производителем биопрепаратов

НИИ ОЧБ

ОЧБ

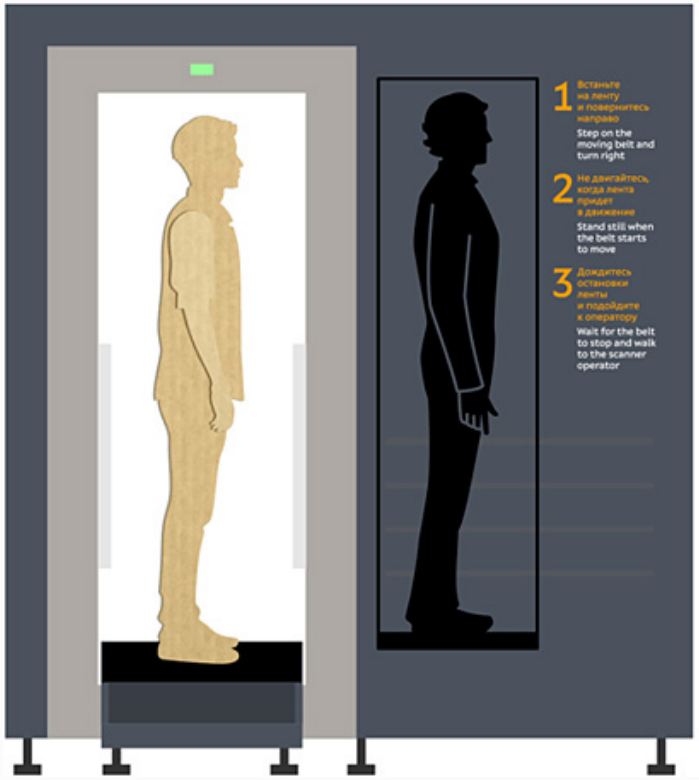
Презентации

- И.В. Чурилова, О.В. Терехов, В.В. Пасов, Н.В. Леонова, Ю.И. Дроздова, Д.А. Егорова, Радиопротекторные свойства препарата Рексод.
- А.И. Кобатов, Н.Б. Вербицкая, О.В. Добролеж, Е.А. Гуреева, И.В. Кутник, Поддержание колонизационной резистентности организма человека как способ снижения медицинских рисков при выполнении космических полетов.
- Т.С. Егорова, А.М. Шляков, Н.В. Конторина, Л.А. Прокофьева, Разработка препаратов для терапии обширных термических ран, осложненных бактериальными инфекциями, различной этиологии, в том числе, вызванных радиационными поражениями.
- А.С. Симбирцев. Рекомбинантные цитокины и иммуномодуляторы в аспекте радиационной и химической безопасности.

План

- разработки
- биопрепараты
  - антиоксиданты
  - иммуномодуляторы
- интраназальное введение

Актуальность



Разработки

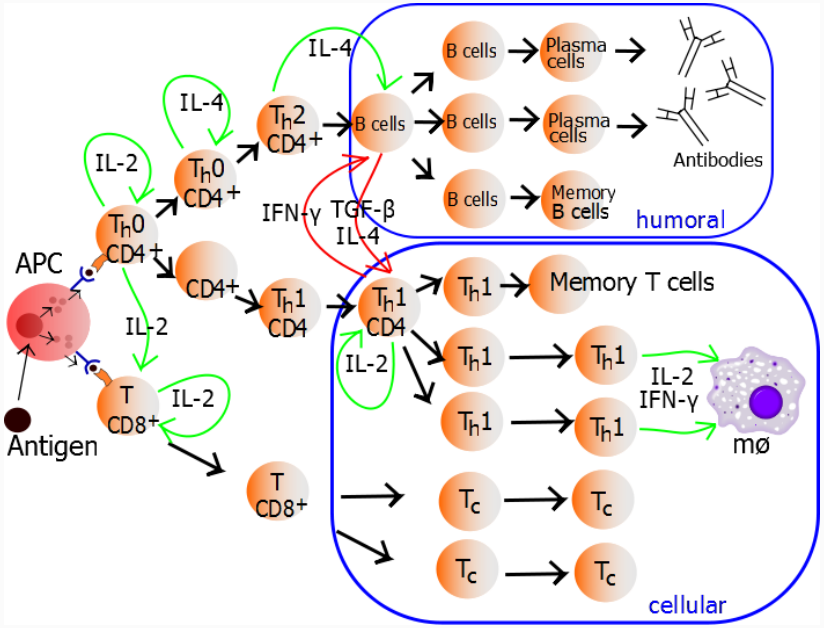
- средства повышения радиорезистентности организма к облучению в субклинических дозах
  - антиоксиданты (СОД)
  - ноотропы и биостимуляторы пептидной природы
- радиомитигаторы иммуномодулирующего действия
  - рекомбинантные и ДНК вакцины
  - цитокины
  - регуляторные пептиды
- биополимеры
  - системы направленной доставки
- сорбенты, гемосорбенты

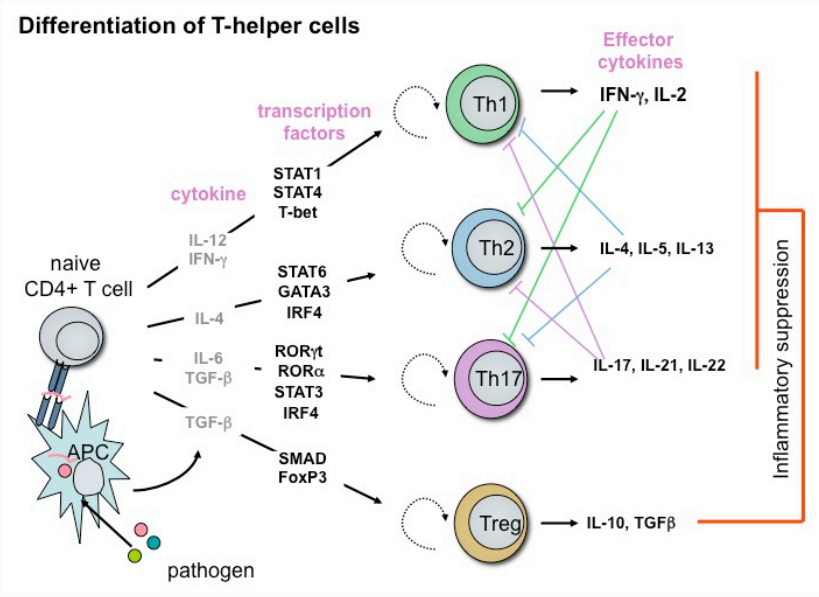
Антиоксиданты

Контроль

Препарат

Иммунный ответ





Цитокиновый шторм

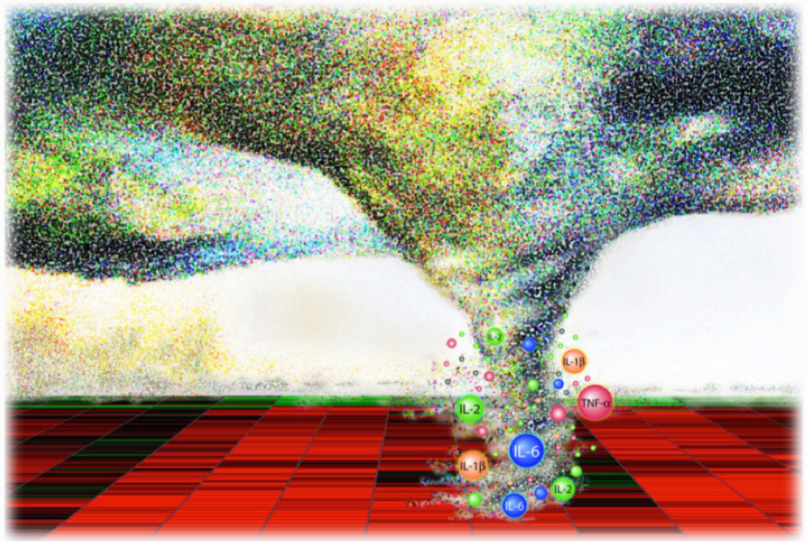
MMBR
Journals.ASM.org

Into the Eye of the Cytokine Storm

Jennifer R. Tisoncik,[a] Marcus J. Korth,[a] Cameron P. Simmons,[b] Jeremy Farrar,[b] Thomas R. Martin,[c] and Michael G. Katze[a]

Department of Microbiology, University of Washington, Seattle, Washington, USA[a]; Oxford University Clinical Research Unit, Wellcome Trust Major Overseas Program, Ho Chi Minh City, Vietnam[b]; and Medical Research Service, Division of Pulmonary and Critical Care Medicine, Department of Medicine, VA Puget Sound Medical Center, University of Washington School of Medicine, Seattle, Washington, USA[c]

INTRODUCTION 16
CYTOKINES 17
Cytokines Associated with the Cytokine Storm 18
Interferons 18
Interleukins 18
Chemokines 18
CSFs 18
TNFs 18
Cytokine Dynamics 18
Regulation of Pro- and Anti-Inflammatory Cytokines 19
THE CYTOKINE STORM 19
Cytokine Storm Pathology 19
Host Susceptibility to the Cytokine Storm 20
GENOMIC VIEWS OF THE CYTOKINE STORM 21
Cytokine Gene Expression Kinetics 21
Hyperresponsiveness of PRRs 22
Differential Host Proinflammatory Responses 23
Key Cytokine Storm Mediators 24
Strength of Chemoattractant Responses 25
Increased Capillary Permeability Syndrome 26
TARGETING THE CYTOKINE STORM 26
Challenges of Current Immunotherapies 26
Implications for Therapeutic Strategies 27
CONCLUDING REMARKS 27
ACKNOWLEDGMENTS 28
REFERENCES 28



Статины

Accepted Manuscript

Treating Influenza with Statins and Other Immunomodulatory Agents

David S. Fedson

PII: S0166-3542(13)00184-8
DOI: http://dx.doi.org/10.1016/j.antiviral.2013.06.018
Reference: AVR 3233

To appear in: *Antiviral Research*

Received Date: 14 February 2013
Revised Date: 19 June 2013
Accepted Date: 25 June 2013

Please cite this article as: Fedson, D.S., Treating Influenza with Statins and Other Immunomodulatory Agents, *Antiviral Research* (2013), doi: http://dx.doi.org/10.1016/j.antiviral.2013.06.018

Адъюванты

Magazine
R422

Obituary

Charles Janeway Jr.

N.A. Mitchison pays tribute to Charles Janeway's contribution to the rapidly developing field of T-cell immunology marked by a prescience that kept his colleagues closely following his work and views about the wider field.

Charlie Janeway, immunologist, a leading authority on the T cell and creator of our present understanding of the link between innate and acquired immunity, died of cancer on April 12 at his home in New Haven at the age of 60.

Charlie obtained his undergraduate and medical degree at Harvard, following in the long family medical tradition. Like other talented young medical scientists at the time of the Korean War he then joined the National Institutes of Health, where William Paul introduced him to the new subject of T-cell biology. After periods of research at Uppsala and Cambridge he moved to Yale in 1977. He became a professor of pathology there in 1983 and later helped found the section of immunobiology. The head of an active research group and author of more than 300 papers, his work touched on nearly all aspects of T-cell function. He wrote the leading textbook of immunology, 'Immunobiology: the immune system in health and disease'.

Charlie's outstanding quality was prescience. His great aim was to understand how the whole immune system fitted together. As his group at Yale grew in size it began to generate a stream of cutting edge papers, each bearing the name of one of his young colleagues as lead author. Yet his main love, one suspects, attached to the single author reviews that he published intermittently. He used them to paint a broad develop, and his peers paid close attention because so often he turned out to have got it right. We who were engaged in immunobiology in the seventies and eighties felt we were playing with ideas as in a card game. Each card denoted a theory and an author, the hands could be dealt in any number of ways, and the game as played by experts could be extremely fast. We came increasingly to depend on Charlie's phrases for guidance in our games.

He... used these reviews to project his own view about how a particular area would develop, and his peers paid close attention because so often he turned out to have got it right.

One of these phrases was 'the good, the bad and the ugly', referring to T-cell development in little secret', referring to the need for adjuvants in many immune responses.

This last phrase has a special resonance. Charlie was delivering the opening lecture at the 1989 Cold Spring Harbor symposium, in which he pointed out that in order for T cells to initiate an immune response they must first be informed by antigen-presenting cells of the presence of pathogens. This could — and indeed at the time did — generate nit-picking about how activated ('memory') T cells didn't need adjuvants, and nor did allo-reacting ones. Charlie, however, took a more positive line, and embarked on a search for the receptors that he predicted would recognise pathogens. In 1997 he, together with Ruslan Medzhitov and Preston-Hurlbert, announced their discovery of a human homologue of the *Drosophila* Toll protein signals that proved able to activate adaptive immunity. That prompted many others to join the hunt for receptors able to recognise patterns rather than antigens on bacteria and viruses, of which many have now been found. Charlie had began his career at a time when the term 'the immune system' entered use to emphasise the need for several kinds of lymphocytes to get together in order to mount an effective defence against infection. It must have been a great satisfaction for him to extend this need to encompass other kinds of cell, most notably macrophages and dendritic cells.

Charlie had many other research interests, many of them concerned with the trimolecular complex of MHC–peptide–TCR responsible for specific (as

Editorial

Adjuvants: no longer a 'dirty little secret', but essential key players in vaccines of the future

Expert Rev. Vaccines 10(1), 1–5 (2011)

Takeshi Arakawa
Molecular Microbiology Group, Department of Tropical Infectious Diseases, Tropical Biosphere Research Center, and Division of Host Defense and Vaccinology, Graduate School of Medicine, University of the Ryukyus, 1 Senbaru, Okinawa 903-0213, Japan
Tel.: +81 [illegible]
tarakawa@[illegible]

"Vaccine research is rapidly moving forward, with the hope that in the future, new types of vaccines will be developed that can exploit new vaccine design strategies."

Vaccines are one of the most successful medical innovations in human history

Antibiotics and vaccines are, undoubtedly, two of the most important discoveries that have been made in medical science to date. Vaccination in particular is considered to be the most cost-effective control strategy for infectious diseases [1], and its effect on mortality reduction may even exceed that achieved by antibiotics [2]. Throughout history, numerous successful vaccines have been developed that are based on attenuation or inactivation of pathogenic organisms and the toxins they produce. Smallpox, measles, mumps, rubella, varicella and oral polio vaccines are all good examples of live-attenuated vaccines. Vaccines that contain killed microbes, such as influenza, polio, Japanese encephalitis, and toxoid-derived vaccines, such as diphtheria and tetanus, are safer to use but generally induce weaker immune responses than live-attenuated vaccines.

New technological advances are needed to target diseases that vaccines are currently unable to reach

The most successful vaccines are those that induce minimal local inflammation and provide protection that has long immunological memory in vaccinated hosts. Aluminum salts are the only adjuvant used in human vaccines since their introduction in the 1920s. Surprisingly, the immunological mechanism underlying this adjuvant was not elucidated until relatively recently [3,4]. It is really quite remarkable that this adjuvant has been in use for more than 70 years without its precise mechanism of action being known. This is a good example of why many immunologists still consider vaccines as mere 'byproducts of luck'. Indeed, in medical history, many successful vaccines were developed empirically using relatively simple methods such as inactivation or attenuation of pathogenic organisms or their components. However, the scope of current and future vaccines has widened tremendously. There are many disorders that cannot be ameliorated by inactivated or attenuated vaccines, including many infectious and autoimmune diseases [5], allergies, cancers and many other conditions such as high blood pressure, dementia and drug dependency. Vaccine research is rapidly moving forward, with the hope that in the future, new types of vaccines will be developed that can exploit new vaccine design strategies.

Biotechnology helps vaccine research rapidly move into a new era of discovery

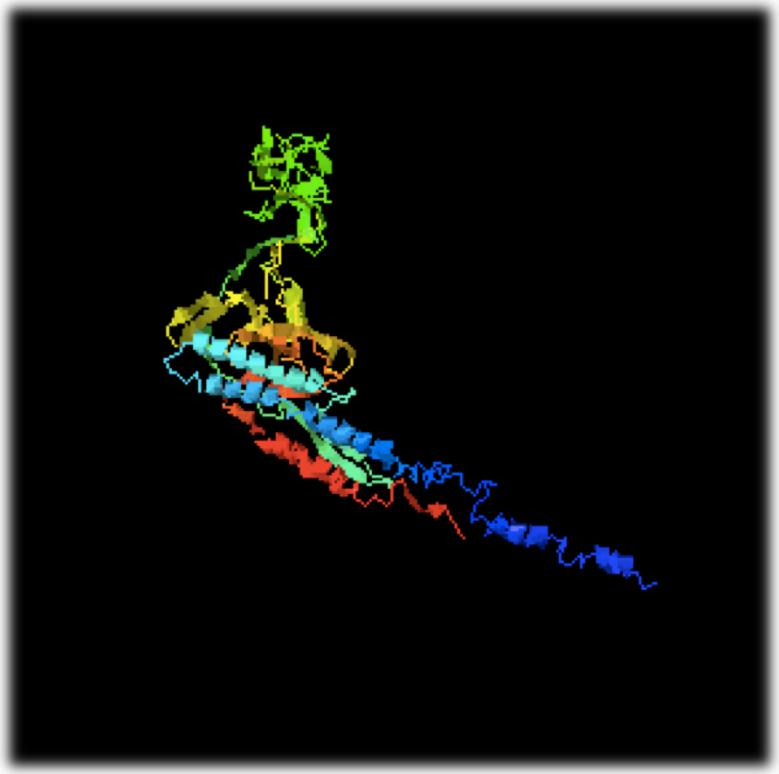
Many potential vaccine-preventable infectious diseases exist that eagerly await vaccine development. However, it is important

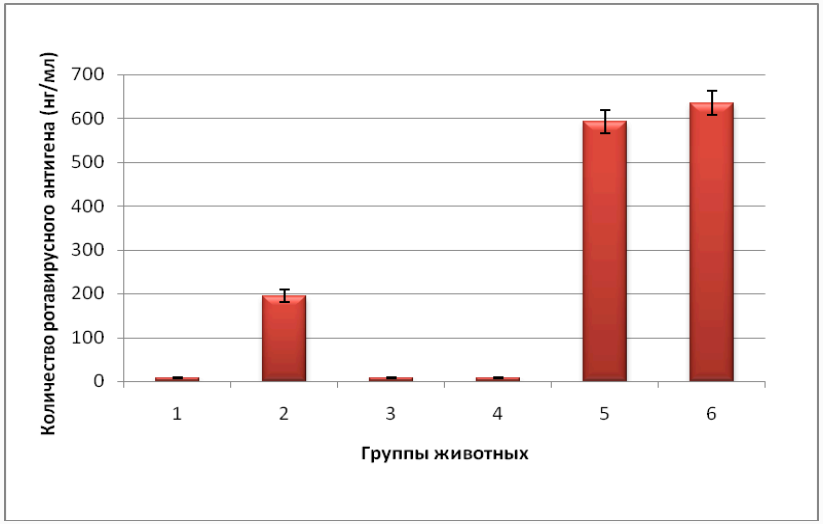
EXPERT REVIEWS

Keywords: adjuvant • antigen-presenting cells • dendritic cells • immunity • pathogen • recombinant protein antigen • vaccine

 10.1586/ERV.10.140 ISSN 1476-0584

Молекулярные адъюванты



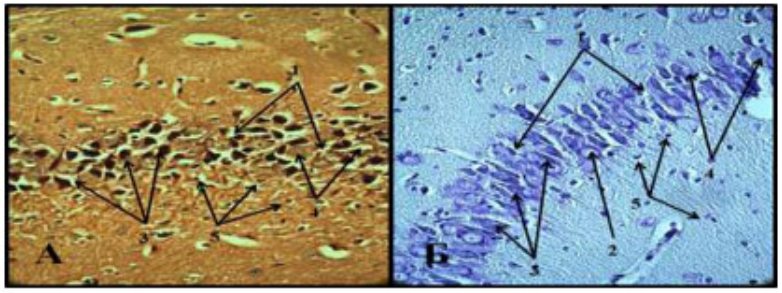


Пробиотики

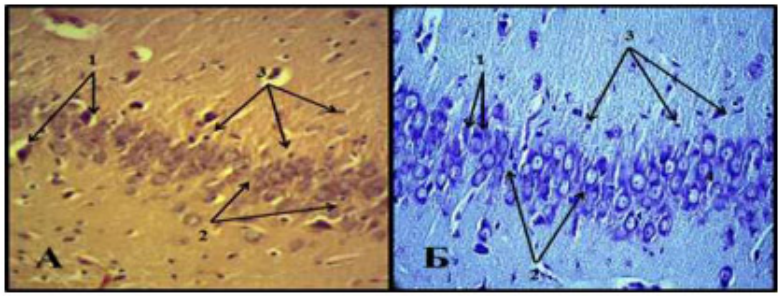

Биологически активная добавка к пище
ВИТАФЛОР®
СИМБИОТИЧЕСКИЙ КОМПЛЕКС
АЦИДОФИЛЬНЫХ БАКТЕРИЙ
пористая масса 230 мг
флаконы №7
2·10⁸
7 флаконов
ПЕРЕД ПРИМЕНЕНИЕМ РЕКОМЕНДУЕТСЯ ПРОКОНСУЛЬТИРОВАТЬСЯ С ВРАЧОМ


ВИТАФЛОР

Нейропротекторы

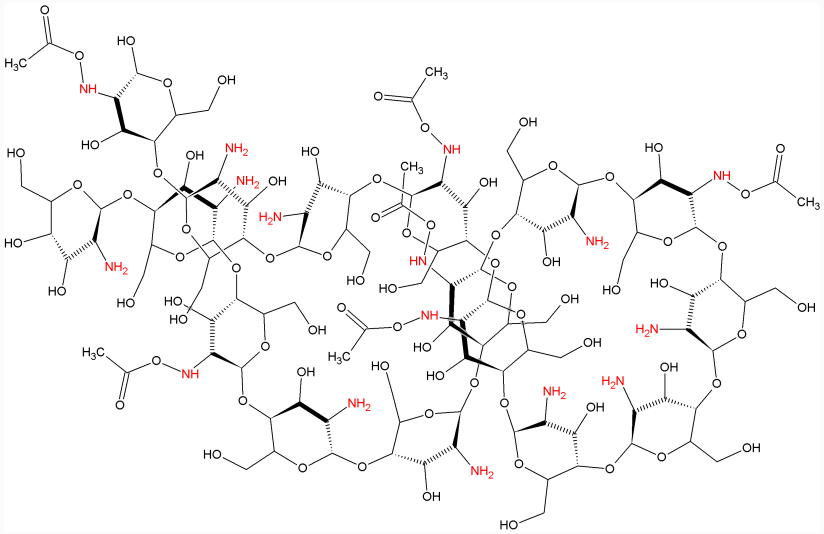


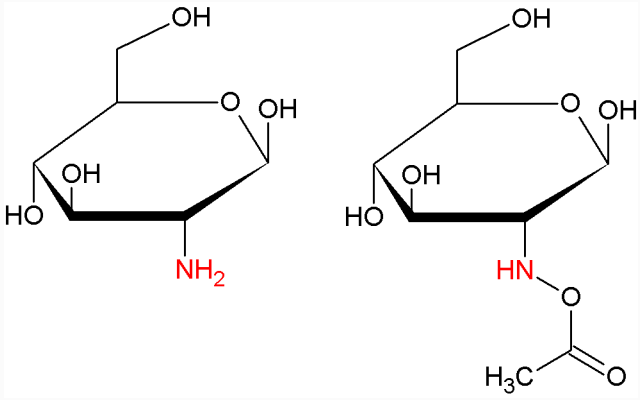
Поле СА3 гиппокампа крыс на 21 сут после воздействия оксида углерода в дозе
0,8 LC50 (окраска гематоксилином и эозином (А), крезиловым фиолетовым по Нисслю (Б),увеличение × 400):
1 - участки очагового выпадения нейроцитов;
2 - изменения хроматофильного вещества ввиде хроматолиза;
3 - глыбчатый гиперхроматоз цитоплазмы;
4 - клетки-тени;
5 - выраженная микроглиальная реакция.



Поле СА3 гиппокампа крыс, получавших в качестве лечения пептид D-лизаргам (40 мкг/кг/сут, 5 дней), на 21 сут после воздействия оксида углерода в дозе 0,8 LC50 (окраска гематоксилином и эозином (А), крезиловым фиолетовым по Нисслю (Б), увеличение × 400):
1 - единичные нейроны с глыбчатым гиперхроматозом цитоплазмы;
2 - единичные клетки- тени;
3 - умеренная микроглиальная реакция.

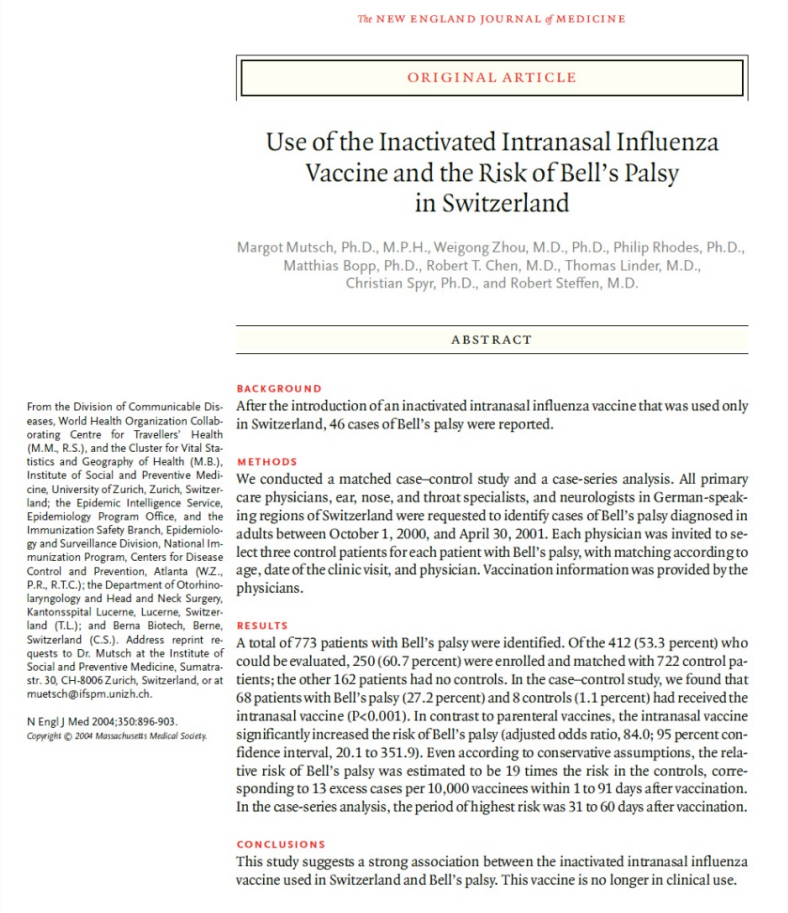
Биополимеры





Интраназальное введение

Интраназальное введение



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Use of the Inactivated Intranasal Influenza Vaccine and the Risk of Bell's Palsy in Switzerland

Margot Mutsch, Ph.D., M.P.H., Weigong Zhou, M.D., Ph.D., Philip Rhodes, Ph.D., Matthias Bopp, Ph.D., Robert T. Chen, M.D., Thomas Linder, M.D., Christian Spyr, Ph.D., and Robert Steffen, M.D.

ABSTRACT

BACKGROUND
After the introduction of an inactivated intranasal influenza vaccine that was used only in Switzerland, 46 cases of Bell's palsy were reported.

METHODS
We conducted a matched case–control study and a case-series analysis. All primary care physicians, ear, nose, and throat specialists, and neurologists in German-speaking regions of Switzerland were requested to identify cases of Bell's palsy diagnosed in adults between October 1, 2000, and April 30, 2001. Each physician was invited to select three control patients for each patient with Bell's palsy, with matching according to age, date of the clinic visit, and physician. Vaccination information was provided by the physicians.

RESULTS
A total of 773 patients with Bell's palsy were identified. Of the 412 (53.3 percent) who could be evaluated, 250 (60.7 percent) were enrolled and matched with 722 control patients; the other 162 patients had no controls. In the case–control study, we found that 68 patients with Bell's palsy (27.2 percent) and 8 controls (1.1 percent) had received the intranasal vaccine ($P<0.001$). In contrast to parenteral vaccines, the intranasal vaccine significantly increased the risk of Bell's palsy (adjusted odds ratio, 84.0; 95 percent confidence interval, 20.1 to 351.9). Even according to conservative assumptions, the relative risk of Bell's palsy was estimated to be 19 times the risk in the controls, corresponding to 13 excess cases per 10,000 vaccinees within 1 to 91 days after vaccination. In the case-series analysis, the period of highest risk was 31 to 60 days after vaccination.

CONCLUSIONS
This study suggests a strong association between the inactivated intranasal influenza vaccine used in Switzerland and Bell's palsy. This vaccine is no longer in clinical use.

From the Division of Communicable Diseases, World Health Organization Collaborating Centre for Travellers' Health (M.M., R.S.), and the Cluster for Vital Statistics and Geography of Health (M.B.), Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland; the Epidemic Intelligence Service, Epidemiology Program Office, and the Immunization Safety Branch, Epidemiology and Surveillance Division, National Immunization Program, Centers for Disease Control and Prevention, Atlanta (W.Z., P.R., R.T.C.); the Department of Otorhinolaryngology and Head and Neck Surgery, Kantonsspital Lucerne, Lucerne, Switzerland (T.L.); and Berna Biotech, Berne, Switzerland (C.S.). Address reprint requests to Dr. Mutsch at the Institute of Social and Preventive Medicine, Sumatrastr. 30, CH-8006 Zurich, Switzerland, or at muetsch@ifspm.unizh.ch.

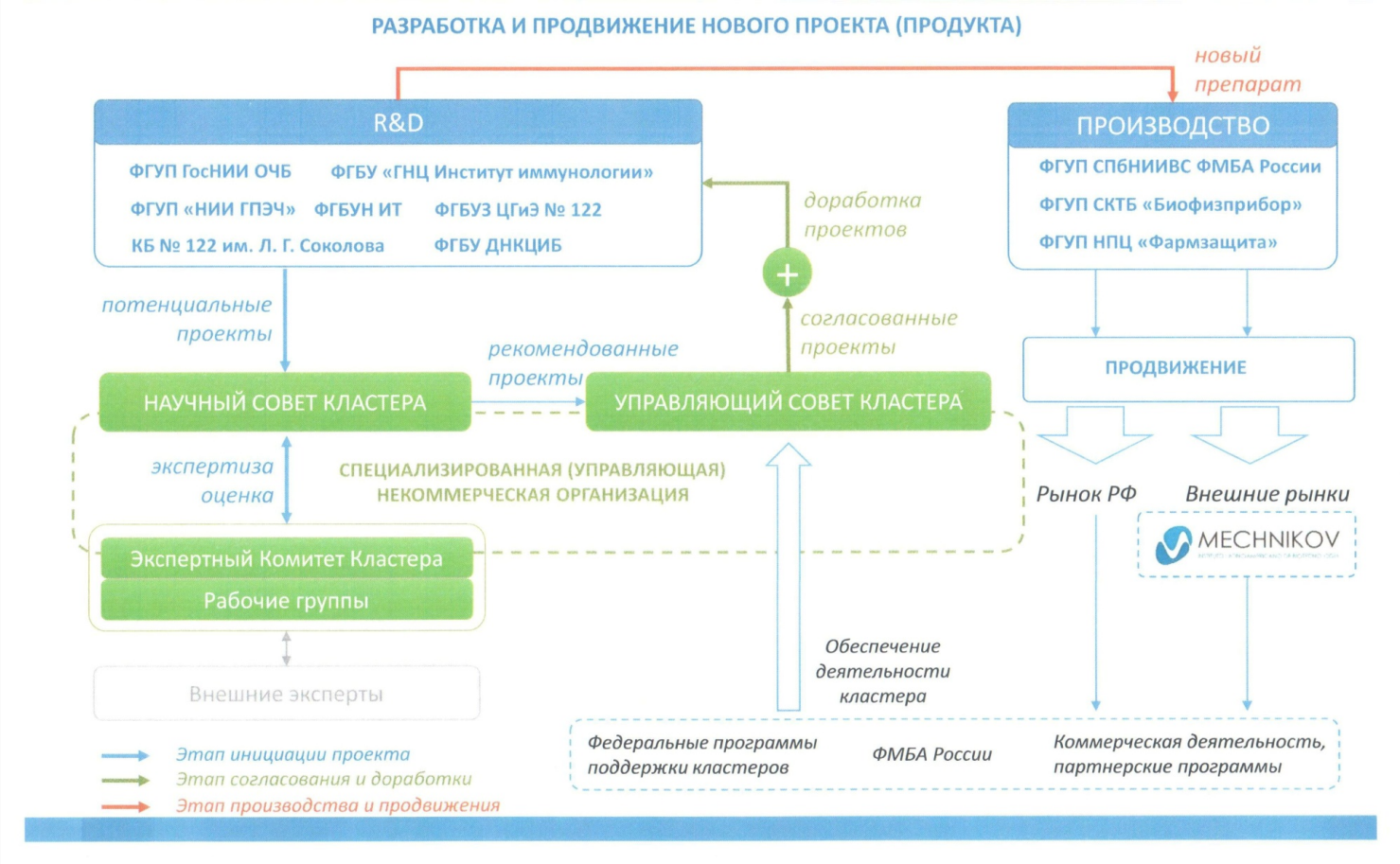
N Engl J Med 2004;350:896-903.

- паралич лицевого нерва у детей
  - в Швейцарии
- вакцина
  - виросомальная
  - интраназальная
  - с мукоадгезивным адъювантом

Дорожная карта

	Разработка	Доклинические исследования	I фаза	II фаза	III фаза
Рекомбинантный рецепторный антагонист интерлейкина-1					
Вакцина против туберкулеза					
Вакцина против ротавирусной инфекции					
Рекомбинантная супероксиддисмутаза					
Белок теплового шока 70					
Рекомбинантный рецепторный антагонист интерлейкина-36					
Ноотропный пептидный препарат					

Кластер ФМБА



НИИ ОЧБ

Заключение

- перспективы биопрепаратов
  - широкий спектр биологической активности
  - новые направления применения
    - уже разрешенные средства!
- комплексный подход
  - потенцирующее действие

НИИ ОЧБ

Спасибо за внимание!