



Head of Department of Problems of interferon and immunomodulators – corresponding member of National Academy of Science of Ukraine, Sc.D., Professor **M. Ya. Spivak** is a well-known specialist in the field of microbiology, virology and immune-biotechnology. Main directions of his scientific activity:

- 1) determination of the fundamental basis of the physiological role of the interferon system and immune regulatory cytokines in norm and in pathology (infectious and inflammatory diseases of bacterial, viral and mixed viral-bacterial genesis, as well as in the case of pre-tumour and tumour diseases induced by carcinogenic viruses);
- 2) optimization of technologies for obtaining new highly effective interferonogenic and antiviral drugs, created on the basis of derivatives and analogues of fluorenones;
- 3) the biotechnological basis for the design of diagnostic test systems for the identification of pathogens of viral and bacterial infections based on recombinant human and animal virus proteins.

The scientific achievements of **M.Ya. Spivak**:

*First established the phenomenon of poly-lysogeny in phytopathogenic bacteria and studied the patterns of interaction of phage bacteria;

*For the first time developed original approaches to the use of cells of lymphoid organs as interferon producing cells;

*Found that when inducing interferons, cells produce other cytokines and low molecular weight defensin-like peptides with antibacterial activity;

*Determined the regularities of the process of induction of cytokines under the action of the original molecular complexes of polybony nucleotides and ligand intercalators;

*Proposed the hypothesis of a universal mechanism of interferonogenesis through local deformation of certain sections of cell membrane with the subsequent inclusion of the regulatory system of secondary cellular messengers;

*Established the key role of the interferon system in the immunopathogenesis of the papillomavirus infection and associated pre-tumour diseases;

*Initiated a new direction in interferonology - the determination of the antibacterial effectiveness of natural interferon preparations and its immunomodulatory ability.

This made it possible to offer new highly effective technologies for the treatment of patients with sepsis, purulent-surgical infections and DVS-syndrome.

*Formulated the concept of the system of interferon and revealed its direct and inverse relationship with the immune and neuroendocrine systems of the organism;

*Developed a methodology for determining the interferon status of the organism, which allows to determine the role and place of the system of interferon on the population level;

*Has established the fundamental foundations of the functioning of the system of interferon in pre-tumour and tumour diseases caused by carcinogenic papillomaviruses.

This made it possible to develop a new direction for targeted stimulation of interferon genesis, based on the original concept of the directed construction of interferon inducers, to add information about the general architecture and morphogenesis of complex animal and plant viruses that are related to one taxon, due to the understanding of the fundamental problems of virology in terms of the evolution of phytopathogenic and zoo pathogenic rbdomoviruses;

*With the help of modern methods of immune biotechnology received interferon preparations of the first and second generations, as well as promising inducers of interferon;

*Defined individual indications and contraindications for the clinical use of interferon drugs and their inducers in viral, bacterial diseases and other pathological processes.

The results of scientific research **M. Ya Spivak** formed the basis of a number of official treatment and prophylactic drugs for humans and animals:

Splenopheron, Leykinpheron, Diapheron, **antiviral drugs** Virex, as well as **immunostimulants** Bifidym, Fitomaks. The biotechnological bases of obtaining recombinant proteins - antigens of hepatitis, AIDS, leukaemia and others have been developed, which allowed to create competitive test systems for clinical diagnosis and to provide the needs of medical institutions of Ukraine.



During the presentation of the D. K. Zabolotny Prize of the National Academy of Sciences of Ukraine

Fundamental results of scientific research of M.Ya.Spivak were awarded with the State Prize of Ukraine in the field of science and technology, the prizes named by D. K. Zabolotny, named by I. I. Mechnikov and named by O.O.Bohomolets and by National Academy of Sciences of Ukraine, silver medal by named I.P.Pavlov (Russia), the gold medal of the World Intellectual Property Organization (Switzerland) and the gold medal of the USSR Supreme Economic Council.

M. Ya. Spivak - author of 436 scientific articles, including 10 monographs, 4 practical manuals and 4

candidate's (PhD) theses have been defended.

Monographs of Mykola Ya. Spivak "Sepsis: Immunology and Immune correction" (2007), "Immune therapeutic Drugs" (2008), "Interferon and the system of mononuclear phagocytes" (2002), "Papillomavirus infection and the system of interferon" (2008), "Interferons: biological and clinical Effects" (2006), Essays on Phagocytosis (2009) filled the information vacuum on these issues.

Among the patents and copyright certificates introduced into the practice of health care and the economy, the most famous are: "Stimulator of immunity in animals", "Method of treatment of purulent-septic diseases", "A method of treatment of acute pneumonia in young children" «Method of obtaining the preparation of interferon», «Inductor of interferon», «Biologically active preparation and method of its achievement», «Method of rehabilitation of patients with radiation damage», «Method of choice of an immune modulator and its optimal dose for correction of immunity in patients», «Method for insulin production" and others.

<http://www.logos.biz.ua/proj/vynahid/online/125.htm>

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Spivak+M+Y>

Danylo Zabolotny Institute of Microbiology and Virology of NASU

Department of Problems of interferon and immunomodulators

The main areas of work are:

- Determination of the fundamentals of interferon and immunoregulatory cytokines physiological role in norm and different pathological conditions (infectious and inflammatory diseases caused by bacteria, viruses or both of them, as well as precancerous and neoplastic diseases induced by carcinogenic viruses).
- Developing of science-based approaches for optimization technologies of obtaining a new high interferonogen and antiviral drugs based on Amixin derivatives and analogues and molecular complexes of single-chain RNA in combination with synthetic monomer intercalators.
- Determination of immunomodulatory properties of new probiotics and prebiotics based on lactic acid bacteria and their derivatives, lectins from bacteria and plants, synthetic muramoyldipeptides etc.



- Development of new biotechnological foundations of diagnostic test-systems construction for viral and bacterial infections causative agents' identification on the basis of human and animal viruses' recombinant proteins.



First was theoretically grounded, experimentally proved and clinically confirmed a new direction in interferonology – determination of interferon antibacterial efficacy in treatment of bacterial infections (sepsis, pyo-septic processes, salmonellosis, toxic shock, etc.). The concept of interferon system was formulated and its direct and inverse link with the immune and neuroendocrine systems of organism was found. A methodology for determination of interferon status, that allows to define the role and place of interferon system at the population level, was identified.



Studies, conducted in the department over the last 5 years, established the fundamentals of interferon system in cases of precancerous and tumour diseases caused by carcinogenic papillomaviruses, allowed to develop a new direction of interferogenesis focused stimulation based on the original concept of compounds (interferon inducers) directed design; added the information about general morphology and morphogenesis of complex animals and plants viruses, that assigned to one taxon, that is concerned with the fundamental problems of virology understanding – phyto- and zoopathogen rhabdoviruses evolution. First and second generation of interferon drugs and promising interferon inducers were received using modern methods of immunobiotechnology. Individually

indications and contraindications for interferon drugs and its inducers clinical use in cases of viral, bacterial diseases and other pathological processes.

The department cooperates with a number of laboratories in USA, Canada, Russia, Israel, Iran, Slovakia and other countries. The department generally prepared 7 ScD and 22 PhD theses, published 11 monographs, 4 practical manuals, 4 guidelines of Ministry of Health of USSR and Ukraine, 2 textbooks, received 84 certificates and patents of USSR, Ukraine and Russia. The technology of α - and γ -interferon drugs obtaining (animaferon, splenoferon, diaferon) was developed. Obtained results were marked by the State Prize of Ukraine in Science and Technology (2005), D.K. Zabolotny National Academy of Sciences of Ukraine Prize (2001), I.I. Mechnikov National Academy of Sciences of Ukraine Prize (2004), O.O. Bogomolets National Academy of Sciences of Ukraine Prize (2010), O. Palladin National Academy of Sciences of Ukraine Prize (2011), Silver Medal of I.P. Pavlov (Russia, 2002), the Gold Medal of the World Intellectual Property Organization (Switzerland, 2002), Gold Medal of the Exhibition of Achievements of the National Economy of USSR (1985), Diploma of Kiev Mayor (2003) and Diploma of the Supreme Council of Ukraine (2007).

It was defined the fundamentals of interferon system and other immunoregulatory cytokines in immunopathogenesis of papillomavirus and herpes infections. There were proposed the new science-based approaches to improve the therapeutic tactics of papillomavirus and herpes infections complex treatment, which include individualized attitude taking into account the clinical and pathogenetic features and microbial associations character, as well as the use of immunotherapy with interferons or their inducers.

To increase the efficiency of herpes simplex virus infections diagnostics "ELISA test system for semi-quantitative analysis and IgG antibodies avidity to herpes simplex virus type 2 determination" was established. A search for new highly effective drugs for alternative antiherpetic therapy was conducted on the experimental models of HSV infection. Such drugs were polycyclic low molecular weight interferon inducers – amixin analogues and derivatives, indolequinolines derivatives.



The innovative developments include the establishment of nanomaterials biological activity (nanocrystalline cerium dioxide, nanoparticles of gold and silver) for viral infections and other pathological conditions, in particular, a

violation of the reproductive function and cardiovascular system insufficiency. Cardioprotective action of gold biosafe nanoparticles was detected and a method of constructing of biosafe and biocompatible nanoconstruction on the basis of gold nanoparticles and cardiotropic drugs with the purpose to increase the efficiency of their targeted delivery in cases of cardio-vascular pathologies was developed. Received conjugate on the basis of cardiotropic drug Simdax and biosafe gold nanoparticles had more effective cardioprotective action, than Simdax drug in cases of experimental doxorubicin-induced heart failure in rats.