THE STEPHAN ANGELOFF INSTITUTE OF MICROBIOLOGY

ASSOCIATED WITH INSTITUT PASTEUR-PARIS

SCIENTIFIC REPORT 2014

Bulgarian Academy of Sciences

The Stephan Angeloff Institute of Microbiology

Associated with Institut Pasteur – Paris

SCIENTIFIC REPORT 2014

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MICROBIAL CELL SURFACE DETERMINANTS OF VIRULENCE AS TARGETS FOR NEW THERAPEUTICS IN CYSTIC FIBROSIS

***Project supervisor*:** A. Molinaro, PhD - Università di Napoli Federico II, Naples, Italy

***Project leader*:** S. Stoitsova, PhD

EU Partners: University of Natural Resources and Life Sciences, Vienna, Austria; Ghent University, Gent, Belgium; Charles University, Prague, Czech Republic; CERMAV-CNRS, Grenoble, France; University of Tuebingen, Germany; Semmelweis University, Budapest, Hungary; Institute of Technology Tallaght, Dublin, Ireland; Università di Napoli Federico II, Naples, Italy; VU University Medical Center, Amsterdam, Netherlands; Institute of Genetics and Microbiology, University of Wroclaw, Poland; Institute for Biotechnology and Bioengineering, Lisboa, Portugal; Universidad CEU San Pablo, Madrid, Spain; Newcastle University and Cardiff University, United Kingdom

This COST Action focuses on the bacterial infections seen in the human hereditary disease Cystic Fibrosis (CF). The disease is associated with organ inflammation and damage particularly affecting the secretory epithelia of the intestine and the lungs. To gain insight into the variety of mechanisms used by bacteria for niche adaptation during chronic infections, one of the aims of the project was to focus on microbe-associated molecular patterns (MAMP). Among these, polysaccharides are of special concern. Within the COST co-operation, we characterized the cyclic enterobacterial common antigen as a novel MAMP candidate. We completed our studies on biofilm formation by the reference strain panel of *P. aeruginosa*. This was our task as a part of the characterization of panel-strain phenotypes. A joint manuscript was completed and submitted. One important objective of the project was the training of young researchers. During 2014 T. Paunova-Krasteva visited Federico II University of Naples, Italy, where she examined the effects of cultivation conditions on the proportions of LPS and ECA at the bacterial surface. D. Borisova joined the training course on "Ion Transport, Airway Liquid Dynamics and Host Pathogen Interactions in CF Lung Epithelia" in Dublin, Ireland. The COST Action BM1003 was ended by a final meeting in October, 2014.

Grant BM1003COST Action

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Final summary

MOLECULAR AND BIOCHEMICAL ANALYZES OF ANTARCTIC STRAINS OF FUNGI: STUDIES ON THEIR BIODEGRADATION ABILITY TOWARD OF PHENOLIC AND POLYAROMATIC POLLUTANTS

Project leader: Z. Alexieva

Project collaborators: Department of Mycology and Department of Microbial Biochemistry – Institute of Microbiology, BAS; Department of General and Applied Hydrobiology of Biological Faculty of University of Sofia; Department of Biotechnology of University of Food Technologies – Plovdiv

Research staff: M. Gerginova, PhD, N. Peneva, J. Manassiev, PhD, A. Sotirova, A. Terziyska, PhD, B. Atanasov, PhD, H. Yemendzhiev, PhD

The taxonomic affiliation of 16 new strains of fungi isolated from Antarctica was determined. These strains were identified at species level by obtaining of 18S rDNA and relevant ITS sequences and were registered in NCBI. Characterization of the tolerance and the biodegradation potential of model and newly-isolated Antarctic fungal strains were accomplished with respect to phenol and hydroxyl and methyl derivatives of phenol. On this basis, were selected 4 strains, representatives of the genus *Aspergillus*, with a high level of biodegradation capacity towards phenol. The highest rate of catechol and *p*-cresol degradation was observed for the strains *A. fumigatus* AL8 and *A. glaucus* AL1. *A. fumigatus* strain AL8 was the most active with respect to the decomposition of *o*-cresol, and *A. fumigatus* AL1 and AL9 are the most effective in the degradation of hydroquinone.The functional properties of key enzymes performing the initial steps of the phenol catabolism of in the cells of the test strains was performed and defined by biochemical analyses. The key enzyme activities - phenol hydroxylase and catechol 1,2-dioxygenase in studied mould strains were defined for the first time. It has been shown that the activity of the investigated enzymes vary significantly depending on the type of the carbon substrate in the culture medium. The strain *Aspergillus glaucus* AL1, which is capable of the most effective degradation of p-cresol shows the highest values of the catechol 1,2 -dioxygenase activity. An alternative enzymatic mechanism of opening of the aromatic ring in the tested strains was established. The tolerance of the all strains tested with regard to the presence of PAH in the growth media was examined. Seven of the tested fungal strains were growing well in a rich medium in the presence of naphthalene, anthracene and phenanthrene. These strains were elaborated for their ability to degrade PAHs. For the first time the functional properties of the key enzymes of the catabolism of aromatic compounds were defined as involved in the biodegradation of naphthalene, anthracene and phenanthrene in the cells of the test strains. The activities of the investigated enzymes vary considerably depending on the metabolic features of the microbial strains used as well as on the type of carbon substrate. Most The strains possessing an optimum combination of the activity of the phenol hydroxylase and

catechol dioxygenase such as the strains and representatives of Aspergillus fumigatus were established as the most active in PAH degradation and utilization. An original molecular analysis for identification, sequencing and comparative analysis of genes encoding phenol hydroxylase and catechol 1,2-dioxygenase in Antarctic studied fungal strains belonging to the genus *Aspergillus* was performed. A mathematical "fuzzi" - model for initial evaluation of the toxicity of the test PAH compounds during the biodegradation process in different strains was created.

Grant DTK 02-74/10 from the Bulgarian Science Fund

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Gerginova, M., Litova, K., Manasiev, J., Peneva, N., Alexieva, Z. (2014). Analyses of enzymes involved in the degradation of catechol and *o*-cresol by *Aspergillus fumigatus* strain, isolated from Antarctic soil. *J. Biotechnol.* 185S S37–S125 S61.

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ISOLATION AND IDENTIFICATION OF *STREPTOCOCCUS THERMOPHILUS* STRAINS FROM ARTISANAL BULGARIAN YOGHURTS

Project leader: G. Stoyancheva, PhD

Research staff: Penka Petrova, PhD; Galina Stoyancheva, PhD

The specific natural and climatic conditions in Bulgaria had contributed for the spontaneous volition of unique strains of Lactic acid bacteria (LAB). There are several regions of the country that are known to contain endemic micro flora taking part in the home-made yoghurt manufacturing. We investigated the microbial diversity of artisan fermented milk products from isolated and remote territory and selected the available *Streptococcus thermophilus* strains. The identification of the isolates to species level was performed by sequencing of ribosomal operon variable regions.

Grant CHR. HANSEN A/S Denmark

MOLECULAR ANALYSES AND NEW APPROACHES FOR MONITORING OF MICROFLORA OF FERMENTED FOODS

Project Leader: S. Danova, PhD

EU Partner*: University of Liege (ULg), Wallonie, Belgium*

Research staff: N. Ivanovska, DSc, R. Tropcheva, PhD, N. Boteva, P. Ganeva and P. Paskova, MSc students,

Different parallel studies of fermented dairy products, traditional for Belgium and Bulgaria obtained from raw milk were realized, according to the scientific program. This allowed the adoption of new approaches for the characterization of lactic acid microflora of traditional cheeses and other dairy products such as "katak" for Bulgaria. For the first time have been implemented metagenomic analyses of Bulgarian cheese made by traditional technology and homemade "katak". A presence of new taxons listed so far in the kingdom Prokaryotes, including the group of lactic acid bacteria (LAB) was established. These data are unique and complete the information on the European microflora of cheeses, including the typical ones for the Balkans.

So far, the project stimulates further research on relationships between microflora and useful properties of Bulgarian MKB from traditional products and points on their application in new functional foods.

As a first form of collaboration between Laboratory of "Lactic acid bacteria & Probiotics" in the Stephan Angeloff Institute of Microbiology and ULg Liege, Belgium, the project will contribute to the further participation in EU collaborative research initiatives.

Bilateral joint project (2012-2015 г.) in the frame of agreement between WBI, Wallonie, Belgium and Bulgarian Academy of Sciences, Bulgaria.

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New projects

MODERN MOLECULAR APPROACHES FOR FUNCTIONAL CHARACTERIAZATION OF THE PROBIOTIC PROPERTIES AND TECHNOLOGICAL CHARACTERISTICS STUDY OF THE AMYLOLYTIC LACTIC ACID BACTERIA FROM BULGARIAN FERMENTATIVE PRODUCTS

Project leader: V. Gotcheva, PhD, University of Food Technologies, Plovdiv, Bulgaria

Project collaborators: The Stephan Angeloff Institute of Microbiology, BAS, Sofia; Institute of Chemical Engineering, BAS, Sofia

Project staff: A. Angelov, PhD, G. Blagoeva; P. Stefanova, P. Petrova, PhD, P. Velikova, A. Stoyanov; K. Petrov, PhD; F. Tsvetanova; L. Popova; E. Vassileva

Grant DFNI B02/27, 2014, NSF

DEPARTMENT OF INFECTIOUS MICROBIOLOGY

LABORATORY OF ZOONOZES AND BACTERIAL VIRULENCE

Final Summary

MOLECULAR EPIDEMIOLOGY, PATHOGENIC POTENTIAL AND DRUG RESISTENCE RANGE OF AEROMONAS *HYDROPHILA* AND *YERSINIA RUCKERI*

***Project Supervisor**:* Petja Orozova, PhD

***Project leader*:** H. Najdenski, DSc,

Project collaborators: Biology Faculty, Sofia University "St. Kliment Ohridski", National Diagnostic and Research Veterinary Institute "Prof. Georgi Pavlov", Sofia

Research staff: I. Tsvetkova, Ms

Epizootic studies on fish farms for clearing up their status related to yersiniosis and aeromonosis were carried out. Strains belonging to the species *Aeromonas hydrophila* and *Yersinia ruckeri* isolated from fishes are characterized morphologically, physiologically, biochemically and genetically. The presence of various virulence factors such as cytotoxins, hemolysins, proteolytic activity and lysine decarboxilase activity is determined. The results are reliable basis for development of diagnostic techniques for rapid identification of virulent *Aeromonas hydrophila* and *Yersinia ruckeri* strains of fish origine. Comparative assays for determination the level of drug resistance to new isolates were performed. After immunization of rabbits are prepared polyvalent antisera for rapid diagnosis of *Y. ruckeri* infection caused by both biotypes - 1 and 2. For the first time in Bulgaria is detected and isolated *Yersinia ruckeri* biotype 2, which is rigid and does not have lipase activity in contrast to biotype 1. Vaccine against *Y. ruckeri* by using biotype 1 and biotype 2 strains isolated from Bulgarian fish farms is developed.

Joint research task between the SAIM-BAS and National Diagnostic and Research Veterinary Institute "Prof. Georgi Pavlov"

SYNTHESIS AND *IN VITRO* ANTIMYCOBACTERIAL ACTIVITY OF NOVEL (-)-FENCHONE AND CAMPHENE-BASED AGENTS

***Project leader*:** Violeta Valcheva, PhD

***Project staff*:** Hristo Najdenski, DVM, DSc, Magdalena Bonovska, DVM, PhD, Georgi Stavrakov, PhD, Georgi Dobrikov, PhD

***Project collaborators*:** Faculty of Pharmacy, Medical University of Sofia, Institute of Organic Chemistry, Bulgarian Academy of Sciences

Despite the availability of highly efficacious treatment for decades, tuberculosis (TB) remains a major global health problem. The widespread transmission of resistant variants of *Mycobacterium tuberculosis*, which does not respond to any of the commercial drugs, threatens health security of both developed and developing world. The urgent need of new antimycobacterial agents and development pathways is becoming more and more apparent. We published a series of papers concerning antitubercular activity of more than 200 new diverse structures, including more than 50 new synthetic chiral compounds derived from natural terpenoids (+)-camphor and (-)-fenchone. Many structures showed promising activity (MIC up to 0.27 μM). Recently, we reported for a new class of anti-TB agents – camphane-based derivatives with nanomolar activity against *M. tuberculosis* strains. The quantitative structure–activity relationship (QSAR) study on 12 compounds revealed several structural requirements for antimycobacterial activity: two hydrogen bond donors, two or three rings and no large branched substituents. We describe the design of a set of nine novel camphane-based derivatives following these requirements. The compounds were synthesized and tested against *M. tuberculosis* strain H37Rv. Four of them showed activities in the nanomolar range, significantly higher than the activities in the initial set. The QSAR study based on all 21 derivatives pointed to two main structural requirements for anti-TB activity: two hydrogen bond donors and a side chain with aromatic ring. Thus we accumulate significant experience in this specific area of medicinal chemistry and drug design and motivate to attempt the development of new active compounds against drug susceptible and resistant *M. tuberculosis* strains.

Grant DMU 02/3 from the Bulgarian Science Fund.

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(2014). Antimycobacterial activity of chiral aminoalcohols with camphane scaffold. *Eur. J. Med. Chem.* 81C, 150-157.

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QUANTITATIVE ASSESSMENT OF EGG-WHITE LYSOZYME IN LAYER HENS TREATED WITH POLYBACTERIAL IMMUNOMODULATOR

Project leader: M. Bononvska, PhD

Research staff: R. Karakolev, L. Sotirov, B. Gyurov, T. Savova, D. Nikolov, A. Angelov

Project collaborators: National Diagnostic and Research Veterinary Medical Institute "Prof. Dr. G. Pavlov", Sofia; Faculty of Veterinary Medicine, Trakia University, Stara Zagora and Hipro Bulgaria OOD

We have traced the dynamics of concentrations of lysozyme in the egg-white of layer hens treated with polybacterial immunomodulator. Experiments had been conducted on two flocks of hybrid Lohmann Brown commercial layers, where from for the entire egg-laying period we took samples to determine the concentration of lysozyme in the egg-white. In both flocks, we observed maximum values in the peak of the laying capacity, followed by a decline after reaching the age of 38 weeks. In the control flock, at the start of laying at the age of 24 weeks, the concentration of lysozyme was 4582.09±229.61 mg/l, thereafter rising to 7549.11±251.62 mg/l at week 34. After that we registered a decrease of values, alongside a decline in the egg-laying capacity. In the test flock, which was being treated with HELPANKAR, as soon as week 24, the concentration of lysozyme was 7391.62±364.85 mg/l, reached its maximum - 11102.88±152.86 mg/l - in week 38, and remained at high levels until week 70 - 5103.17±222.21 mg/l. These data indicate that, given an appropriate stimulation of the mucosa with a polybacterial immunomodulator, the immune system of the birds responds with an increased production of lysozyme in the egg-white, conversely to what had been found in the control flock. Eggs produced thereby have, on the one hand, increased nutrition value, and on the other, they are a precious raw material for processing and extraction of the lysozyme because they contain approximately twice as much lysozyme compared to the physiological norm.

Joint research task between the SAIM-BAS and National Diagnostic and Research Veterinary Institute “Prof. Georgi Pavlov”

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TRANSNATIONAL ENHANCEMENT OF ECOPORT 8 NETWORK

Project leader: J. Marinski, PhD (NIMH-BAS)

EU partners:

- **Universities and Research Institutes** - Polytechnic University of Bari; National Institute of Meteorology and Hydrobiology, Bulgaria; Universus CSEI, Training and Innovation University Consortium, Italy; Polytechnic University of Tirana; Institute of Marine Biology, University of Montenegro; National Institute of Marine Geology and Geoecology, Romania; Technological Educational Institute of Epirus; Greece)
- Port **Authorities or Port Managing Bodies** of Bar, Bari, Bourgas, Brindisi, Dubrovnik, Durres, Igoumenitsa, Patras coming from seven countries of the South East Europe (SEE) area

Research staff: Z. Tsvetanova, PhD

TENECOPORT (http://www.tenecoport.eu/) involved Mediterranean and Black Sea ports in South East Europe with aim to improve the quality of ports management, placing the prevention of pollution and preservation of natural resources in port areas and nearby coastal zones as pivotal to the maritime system.

Launched in October 2012 and concluded in December 2014, the TEN ECOPORT project was aimed at capitalizing the ECOPORT 8 project results and provision of a Common Model of Environmental and Sustainability Development and Sustainable Accessibility of the sea-networks. The developed TEN ECOPORT Platform ensured sustainable development of the sea-corridors through implementation the Environmental Management System in the ports and creation the first port network for development, strengthening and transfer of coordinated cooperation initiatives for eco-management of the sea routes.

The efforts of the BG team were focused on the port of Bourgas, including eco-mapping of specific critical issues and vulnerability risks within the Bourgas port and surrounding area, monitoring the water quality in the Bourgas port, development of GIS information system and shared guidelines for eco-management of the ports.

Grant Ten Ecoport, Code SEE/D/0189/2.2/X South East Europe Transnational Cooperation Programme, Priority Axis 2. Protection & Improvements of The Environment; Area of Intervention 2.2. Improve Prevention of Environmental Risks

References:

Tsvetanova, Z., Korsachka, M., Marinski, J. (2014). Water quality assessment of the Bourgas port waters, In: *Sustainable Development of Sea-Corridors and Coastal Waters* (Eds. S.Chrysostomos, T.Floqi, J.Marinski, L.Damiani), Springer International Publishing, Switzerland, pp. 250 (in press)

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Current Project

PREVALENCE OF HUMAN PATHOGENIC *YERSINIA ENTEROCOLITICA* IN TONSILS OF SLAUGHTER-AGED PIGS

***Project supervisor*:** H. Najdenski, DSc

Project collaborators: Unit "Food Safety", Institute for Agriculture and Fisheries Research (ILVO), Melle, Belgium

Research staff: M. Gatzovska, Ms, M. Zaharieva, PhD, T. Dimova, PhD, I. Tsvetkova, Ms, T. Draganova, Ms, L. Dimitrova, Ms

The object of this study was to obtain prevalence data for human enteropathogenic *Yersinia entercolitca* on tonsils in slaughter-aged pigs in Bulgaria and regional distribution of this prevalence. Tonsil samples from 201 slaughter pig, originating from the regions of Sofia, Stara Zagora and Shumen were examined for the presence of pathogenic *Yersinia enterocolitica*. Two days enrichment method in Peptone Sorbitol Bile Salt broth at 26^{o}C was applied, followed by streaking on selective cefsulodin-irgasan-novobiocin (CIN) agar after alkali treatment. Typical colonies were confirmed by biochemical methods and DNA isolation of crude cell lysates was carried out. For the PCR identification specific primers for 16SrDNA and chromosomal *ail* gene for *Y. enterocolitica* and *Y. pseudotuberculosis* were applied (according Lambertz, 2008).

Of the tested pigs 9.5% were found positive for *Yersinia enterocolitica* and 4% proved as pathogenic bioserotypes. The percentage of positive pigs of human *Y. enterocolitica* pathogenic strains per batch varied. Prevalence was shown to be significantly higher in Shumen's region. No bacteria from the species *Y. pseudotuberculosis* were detected.

In conclusion, the low rate of pathogenic strains in slaughter pigs, does not exclude the importance of *Yersinia enterocolitica* hazard. At slaughter level, classical tonsils detection of *Yersinia enterocolitica* accompanied by molecular identification, quantification and typing should be performed.

Belgian-Bulgarian Bilateral project

GEIGERIA ALATA (DC.) – A NEW SOURCE OF BIOACTIVE COMPOUNDS

***Project supervisor*:** G. Momekov, PhD, Medical University of Sofia

Project leader: H. Najdenski, DSc

***Project partners*:** Department of Pharmacology, Pharmacotherapy and Toxicology, Department of Pharmacognosy and Botanics, Faculty of Pharmacy, Medical University of Sofia, Department of Infectious Microbiology, The Stephan Angeloff Institute of Microbiology, BAS

***Research staff*:** M. M. Zaharieva, PhD, I. Tsvetkova, MS

Geigeria alata (Asteraceae) is a traditional plant used in Sudanese folk medicine for treatment of diabetes, cough, epilepsy, intestinal complaints for a long time. Seven phenolic acids: protocatechuic (**1**), neochlorogenic (**2**), chlorogenic (**3**), caffeic (**4**), 1,3-dicaffeoylquinic (**5**), 3,4-dicaffeoylquinic (**6**) and 1,3,5-tricaffeoylquinic acids (**7**) were analyzed for the first time in roots and leaves extracts of *G. alata* using HPLC-UV. Ultrasound assisted extraction of samples with 80 % methanol allowed a good recovery of the analytes: from 92.54% (**1**) to 102.40% (**3**). The subsequent HPLC quantification was achieved using a Hypersil ODS C18 column and UV detection at 280 nm and 310 nm. The mobile phase consisted of water and methanol, and gradient elution mode was applied. The detection limits ranged from 0.04 μg/ml (**1** and **2**) to 0.57 μg/ml (**5**). *G. alata* roots revealed higher total amount of phenolic derivatives (11.5±0.14%) and lower level of total flavonoids (7.56 ± 0.06%) compare to leaves. **5** was the dominant compound in roots (25.96 ± 2.08 mg/g dry extract), while **6** was the major phenolic acid (8.99 ± 0.56 mg/g) in leaves. *G. alata* roots demonstrated significantly strong DPPH radical-scavenging activity (IC_{50} 53.98 μg/ml) and FRAP potential (268.60 ± 4.63 μM TE/mg dw). The antibacterial activity against *S. aureus* (MIC, MBC 1.25 mg/ml), *MRSA* (MIC, MBC 1.25 mg/ml), *B. subtillis* (MIC, MBC 0.63 mg/ml) was estimated using the broth microdilution method and could be of relevance for eventual topical application by skin infections. *G. alata* is a good new source of bioactive compounds.

Grant 238/14.01.2015, Medical University of Sofia.

LABORATORY OF ANTIMICROBIAL AGENTS

Current project

WATER-SOLUBLE PHTHALOCYANINES FOR FLUORESCENCE DIAGNOSIS AND PHOTODYNAMIC THERAPY

***Projekt supervisor*:**M. Durmuş, Gebze Institute of Technology, Turkey

***Projekt leader*:** V. Mantareva, PhD, Institute of Organic Chemistry with Centre of Phytochemistry, BAS

Research staff: V. Kussovski, PhD, I. Angelov, PhD

A series of silicon(IV) phthalocyanines axially substituted with methylparaben, ethylparaben, propylparaben and butylparaben groups were synthesized and studied as photosensitizers for antimicrobial photodynamic therapy. The absorption, fluorescence, photodegradation and singlet oxygen generation properties of the synthesized Si(IV) phthalocyanines were studied. In vitro antibacterial photodynamic therapy was investigated against cariogenic pathogenic bacterium Streptococcus mutans. Axially propylparaben substituted Si(IV) phthalocyanine showed significant photodynamic efficacy (log 4) at concentration of 10 mM and mild irradiation (60 mW cm^2, 50 J cm^2, LED 637 nm). The low inactivation capacity was observed for the other studied Si(IV) phthalocyanines. The uptake and localization properties of axially propylparaben substituted Si(IV) phthalocyanine showed a sufficient level of accumulation in planktonic cultured bacterium and a complete penetration depth into the biomass of the 48-h bacterial biofilm.

Grant No: 212M053, Joint research project TUBITAK – BAS

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DEPARTMENT OF APPLIED MICROBIOLOGY

LABORATORY OF MICROBIAL BIOSYNTHESIS AND ECOLOGY

Final Summary

BIOTECHNOLOICAL AND ECO-FRIENDLY APPROACH FOR EFFECTIVE UTILIZATION OF WASTE PLANT BIOMASS FOR COMPOST AND SOIL IMPROVEMENTS

Project leaders: A. Gousterova, PhD and K. Tsekova, PhD

Project collaborators: Inovet OOD, Sofia

Research staff: H. Najdenski, DVM, DSc, D. Todorova, PhD, D. Paskaleva, MS, I. Tzvetkova, MS

In the project, cheap and harmless bioproducts, compost and soil conditioner, have been obtained from greenhouse plant waste materials: tomatoes and pepper leaves and stems, corn cobs and vine sticks. A method has been developed for more effective utilization of these wastes based on enzyme hydrolysis of the lignocellulose biopolymers by mixed culture of selected microbial strains. Optimal conditions of the biohydrolysis process have been established such as sample size, temperature, pH, humidity, and aeration mode. The effectiveness and safety of the newly obtained bioproducts as fertilizer and soil fertility conditioner have been demonstrated.

Grant BG161PO003-1.1.06 from the Operational Programme "Development of the Competitiveness of the Bulgarian Economics", EU, European Regional Development Fund.

ANAEROBIC BIODEGRADATION OF LIGNOCELLULOSIC WASTES IN ORDER TO PRODUCE BIOGAS AND UTILIZATION OF CARBON DIOXIDE IN IT BY USING MICROALGAE

Project leader: A. Kroumov, Ph.D.

Research staff: I. Simeonov, PhD, D. Galabova, PhD, D. Denchev, PhD, A. Sotirova, MS, E. Chorukova, PhD, S. Mihaylova, MS, V. Hubenov, PhD student, I. Lazarkevich, MS

The main objective of the project to absorb carbon dioxide from biogas by using microalgae and as a result obtaining of biogas with a higher content of methane. The other task was to develop and to study an integrated biotechnological process for the anaerobic biodegradation (AB) of the lignocellulosic material (LM), alone or in a mixture with other organic waste including algal biomass. The following tasks will be solved: laboratory testing of the process to absorb carbon dioxide from biogas by using

closed photobioreactor (PBR), study of the algal biomass (AB) as a co- substrate for the production of biogas; choosing of LM pre-treatment method in order to facilitate their maximum digestion ; studies (laboratory and pilot conditions) on obtaining biogas from LM. To formalize the kinetics of algal physiology in closed PBR, the methods of mathematics will be applied. Algae strains resistant to high concentrations of carbon dioxide have to be isolated and selected. Results 2014: Algal strain tolerant to high CO2 content in the gas phase was selected. The complete CO2 utilization from simulated and real biogas by using this strain was achieved in innovative PBR. The 10th new highly effective closed tubular PBRs for laboratory studies were developed and successfully used for the purposes of the biogas purification from CO2. Two PBRs in series were successfully applied in biogas purification process and mathematical model to describe their functioning in the scheme was developed.

Grant DFNI-E01/0001 from the National Science Fund, the Republic of Bulgaria

CULTIVATION OF MICRO-ALGAE IN INNOVATIVE PHOTO-BIOREACTOR FOR CARBON DIOXIDE SEQUESTRATION FROM INDUSTRIAL WASTE GASES FROM DIFFERENT SOURCES AND SYNTHESIS OF HIGH VALUE PRODUCTS

***Project leader*:** A. Kroumov, PhD

***Project collaborators*:** West Parana State University, Department of Chemical Engineering.

Technological lines based on innovative ideas are designed to minimize global warming caused by the accumulation of carbon dioxide from industrial waste gases. In this context, the use of microalgae for scrubbing CO_2 from exhaust gases (exhaust gases from the combustion of organic materials, waste gases from fermentation, etc.) is very attractive because of their great potential and synthesis of high-value products (biologically active compounds BAC). On the basis of an effective system in terms of integrated value, is expected to be solved environmental problems as well as problems related to human health. In this biotech field are concentrated efforts of European programs, as well through HORIZON 2020. **Results-2014:** Algal strains tolerant to high CO2 content in waste gases were isolated from Brazilian lakes and water sources. Preliminary experiments with the most promising isolated strains were performed. A Lab for culturing algae was set up in West Parana State University of Toledo, PR, Brazil.

Grant "Special Visiting Researcher" under the program "Science without Borders"

New project

EFFICIENT USE OF BIOMASS FOR ENERGY AND ENVIRONMENTAL OBJECTIVES: THE POTENTIAL OF BIOETHANOL AS A FUEL FOR RAW MATERIALS

***Project leader*:** S. D. Ivanova, PhD

Research staff: A. Kroumov, PhD

Grant E02/1 from the National Science Fund, the Republic of Bulgaria

LABORATORY OF EXTREMOPHILIC BACTERIA

New project

BIODIVERSITY OF HALOPHILIC MICROORGANISMS ISOLATED FROM BULGARIAN SALT NICHES AND THEIR EXOPOLYSACCHARIDE SYNTHESIS POTENTIAL

Project supervisor: M. Kambourova, DSc

Project collaborators: University of Food Technologies

Research staff: E. Tonkova-Vasileva, PhD, N. Radchenkova, PhD, I. Tomova, PhD, I. Boyadzhieva, PhD, S. Vasilev, MSc.

Grant DFNI 02-26/2014 from the National Science Fund, the Republic of Bulgaria

LABORATORY OF APPLIED BIOTECHNOLOGIES

Final Summary

FLOWCYTOMETRY-APPLICATION IN BIOTECHNOLOGY

Project supervisor: A. Vutsova, PhD

Project leader: Y. Stoykov, PhD student

Project staff: Y. Stoykov, PhD student

Project was performed in aim to encourage young in their work. During the project general knowledge about flowcytometry was obtained. Measurement of colloidal chitin particles were performed, as well as different fluorescent dyes were tested for staining of chitin. It was developed a method for determination of bacterial biomass in cultural fluid in presence of colloidal chitin. It allowed making correlation between chitinase production and biomass growth.

Grant BG051PO0001-3.3.05-0001 "Science and Business" from Ministry of Education and Science.

IDENTIFICATION OF BACTERIAL ISOLATES BY METHODS OF MOLECULAR BIOLOGY

Project supervisor: A. Vutsova, PhD

Project leader: Ts. Teneva-Angelova, PhD student

Project collaborators: Wallenberg Laboratory for Cardiovascular Research, Center for Cardiovascular and Metabolic Research, The Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden

Research staff: Ts. Teneva-Angelova, PhD student

The project target was identification of lactic acid bacteria, isolated from medicinal plants. In recent years there is a trend of increased interest in LAB, isolated from non-dairy origin, due to their diverse metabolic profile and unique flavor-forming activities. Each specified plant species provides a unique environment and allow growth of typical epiphytic flora.

The lactic acid bacteria isolated from medicinal plants were identified by 16S rDNA – based molecular techniques. Fragments of the 16S ribosomal gene were amplified using universal primers 27F (5'-AGAGTTTGATCCTGGCTCAG-3') and 1492R (5'-TACGGTTACCTTGTTACGACTT-3'). Representatives of genera *Lactobacillus*, *Lactococcus*, *Streptococcus* and *Enterococcus* were identified.

Grant BG051PO001–3.3.05–0001 "Science and business", funded on Operational Programme "Human Resources Development"

COMPLEX EVALUATION OF THE CYTOTOXIC EFFECT OF HARPAGOSIDE

Project supervisor: A. Vutsova, PhD

Project leader: A. Marchev, PhD

Research staff: A. Marchev, PhD

The genus *Verbascum* (mullein) is a representative of the family Scrophulariaceae and accounts about 360 species, widely used in Bulgarian traditional medicine for treatment of inflammations, respiratory an oncological diseases.

Among the substances founded in relatively high amounts (~0.5% of the dry weight) in *V. nigrum* (dark mullein) is harpagoside (iridoid glucoside). Harpagoside possess important pharmaceutical activities and is currently listed in the contents of many drugs used for the treatment of arthritis, osteoporosis and heart disease. This is due to its ability to prevent the progress of inflammation processes. Similar processes are running in different cancers, which determine the potential of harpagoside for their treatment.

Harpagoside was isolated and purified from the aerial parts of *V. nigrum*. Its structure was elucidated by Nuclear Magnetic Resonance (NMR) and the purity (≥ 95%) was determined by High Performance Liquid Chromatography (HPLC). The cytotoxicity of harpagoside against different leukemia cell lines (Jurkat, K562, U937 and Raji) as well non-cancerous cell line - peripheral blood mononuclear cell (PBMC) was determined. The IC_{50} values at which harpagoside suppress the growth of the cancer lines Jurkat and K562 have been determined. The performed investigations reveal, that harpagoside has relatively cytotoxic potential. In Jurkat cell line the cell viability could be decreased to 36.99 % when harpagoside was used at 500 μM concentration after 48 h. To decrease the viability of K562 were necessary even higher concentrations of 1000 μM after 72 h of treatment. Although these high concentrations, even at 500 μM, harpagoside had weak cytotoxicity against PBMC cells after 48 h treatment. The compound was also not able to inhibit the NF-kB transcription factor. These results show that harpagoside might have higher potential in prevention of cancer, than in suppressing the cancer growth.

Grant D04-111/28.03.2014 from Operational program "Development of human resources", co-funded by the European Social Fund of the European Union. Project № BG051PO001/3.3-05-0001 „Science and Business".

Current projects:

RATIONAL PLATFORM FOR HALOGENATION OF HIGH-VALUE PHENYLETHANOID GLYCOSIDES FROM PLANT ROOT CULTURE

Project Leader: M.I. Georgiev, PhD

Project Fellows: A. Marchev, PhD, S. Rusinova-Videva, PhD

The aim of the project "Rational platform for halogenation of high-value phenylethanoid glycosides from plant root culture" is to set to work the expertise of the

project partners in the field of plant biotechnology, molecular biology and natural products chemistry in order to elaborate a technology platform for studying verbascoside (and concomitant phenylethanoid glycosides) halogenation in the plant cell/tissue factory. This platform includes the *in vitro* plant tissue culture systems (hairy roots), metabolic engineering, metabolomics and evaluation of bioactive properties of the *Verbascum*'s phenylethanoid glycosides.

Grant DNTS Germany 01/8 (2014-2016)

RATIONAL PLATFORM FOR SUSTAINABLE PRODUCTION OF PHARMACEUTICALLY RELEVANT MOLECULES FROM PLANTS AND THEIR *IN VITRO* CULTURE

***Project supervisor*:** M. Popova, PhD

***Project leader*:** M.I. Georgiev, PhD

***Project staff*:** P. Dimitrova, A. Marchev, PhD; S. Rusinova-Videva, PhD; V. Milanova, G. Zahmanov, K. Georgieva, E. Genova

Chronic (systemic) inflammation and malignant neoplasms are socially-significant diseases, which affect millions of people worldwide. Chemotherapeutic agents currently in use in the clinics did not succeed in fulfilling their expectations even though they are very cost-intensive. In parallel, there is an increasing evidence for the potential of plant-derived secondary metabolites on the inhibition of different steps of tumorigenesis and associated inflammatory processes, underlining the importance of these products in cancer prevention and therapy.

The major scientific impact of the project will be in strengthening of the knowledge on biosynthesis of pharmaceutically relevant phenylethanoid and iridoid glycosides, which will offer an effective tool for management and better "exploitation" of *Verbascum* and *Veronica* secondary metabolism and thus the development of so-called "plant cell/tissue factories".

In order to fulfil the project aims a collaboration consortium, which consists of three academic partners from Bulgaria (Institute of Microbiology, Institute of Organic Chemistry with Centre of Phytochemistry and University of Sofia) and United Kingdom, was established. The project is not only designed to produce novel research findings, but also to help strengthen individual and institutional research capacities.

Grant DFNI B02/14 (2014-2016) from the National Science Fund, the Republic of Bulgaria

Pending support

COMPLEX ASSESSMENT OF DONOR GENOTYPES AND APPROACH FOR CREATION OF BULGARIAN SORTS TOMATOES WITH IMPROVED ANTIOXIDANT CONTENT AND TASTE OF THEIR FRUITS

***Project supervisor*:** B. Bojinov, PhD
***Project leader*:** A. Pavlov, DSc.
***Project staff*:** I. Ivanov, PhD, T. Gocheva, E. Genova

Grant DFNI-B01/16-1012 from National Fund for Scientific Research, Republic of Bulgaria

APPLICATION OF OMICS TECHNOLOGIES TO REVEAL HEALTH POTENTIAL OF BULGARIAN HONEY

***Project supervisor*:** M. Shishinjova, PhD
Project leader: Prof. A. Pavlov, DSc.
Project staff: A. Marchev, R. Vrancheva

Grant DFNI-B01/31-1012 from National Fund for Scientific Research, Republic of Bulgaria

RESARCH GROUP OF MATHEMATICAL MODELLING AND COMPUTER METHODS

Current projects

A STUDY OF ANAEROBIC BIODEGRADATION POSSIBILITIES FOR ORGANIC WASTES ON BOARD THE INTERNATIONAL SPACE STATION

***Project leader*:** I.Simeonov, PhD

***Research staff*:** D. Galabova, PhD, P. Angelov, PhD, D. Denchev, PhD, V. Kasovski, PhD, S. Mihaylova, V. Hubenov

Thermophilic anaerobic strain of *Clostridium thermocellum* (growing at 55 ° C) of the lyophilized form was recultivated In IMicB-BAS. Several recultivation have been done which established the viability of this strain. Several tubes were stored in frozen form with cryoprotectant.

Bilateral joint project in the frame of agreement between Bulgarian Academy of Sciences, and Russian Academy of Sciences

ERASMUS+ AVEC L'UNIVERSITÉ DE LILLE (FRANCE)

***Project leader*:** I.Simeonov, PhD

***Teaching activity* of I. Simeonov from 21.09.2015 till 30.09.2014**

Content of the teaching programme:
1. Mathematical modeling of biotechnological processes
2. Parameters and states estimation
3. Optimisation and control of biotechnological processes

Grant: European Union, Erasmus+

New project

NEW ECOTECHNOLOGIES FOR BIODEGRADATION OF ORGANIC WASTE WITH HYDROGEN AND METHANE PRODUCTION

Project leader: I. Simeonov, PhD

Research staff: H. Naidenski, DSc, M. Angelova, DSc, E. Chorukova, PhD, E. Krumova, PhD, V. Kasovski, PhD, L. Kabaivanova, PhD, N. Kostadinova, PhD, S.Mihaylova, MS, V. Hubenov, PhD, L. Dimitrova. PhD student.

Grant: DFNI-E02/13 from National Fund for Scientific Research, Republic of Bulgaria

DEPARTMENT OF VIROLOGY

Current Projects:

A NOVEL APPROACH TO HIGHLY EFFICIENT CHEMOTHERAPY OF ENTEROVIRAL INFECTIONS

***Project leader**:* Angel S. Galabov, MD, DSc

***Research staff*:** I. Nikolova, PhD; A. Stoyanova, MS; P. Grozdanov, PhD; N. Petrov, PhD; Y. Abashev, PhD; S. Philipov, PhD; N. Vilhelmova-Ilieva, PhD; L. Mukova, MS; N. Nikolova, MS; P. Stoyanova, DVM; Nikolaeva-Glomb, MD, PhD; I. Zahova; E. Dimitrova

***Research collaborator*:** M. Arita, MD, PhD, National Institute of Infectious Diseases, Gakuen, Tokyo

The effect of the combination pleconaril + MDL-860 + oxoglaucine (PMO) following the consecutive alternating administration (CAA) course was tested in experimental neuroinfection infection with Coxsackievirus B1 in newborn mice. In parallel, the activities of the PMO combination applied simmultaneosly and of the monotherapies by the substances partners in the combination was studied, as well. It was established a pronounced protective antiviral effect of the combination PMO via CAA course, in contrast with lack of activity of PMO combination administered every day simmultaneously. The monotherapies with MDL-860 and oxoglaucine were also ineffective, while the pleconaril monotherapeutic course manifested certain activity. Brain samples has been taken for analysis of the phenotypic marker MIC50.

In recent years, phosphatidylinositol 4-Kinase III Beta (PI4KB) has emerged as a conserved target of potent anti-picornavirus compounds including enviroxime. Synthesized selective PI4KB inhibitors with a variety of chemical structure have been developed.

First, we re-evaluated the anti-PV activity of oxoglaucine, which is an aporphinoid alkaloid isolated from Glaucium flavum Crantz. We found that EC50 of 0.51 μM in PV1pv infection and CC50 of 33 μM in RD cells, which were comparable to those of previous reports for PV infection: EC50 of 0.12 μM for PV1(Mahoney), respectively 0.43 μM. for PV1 (LSc-2ab), and CC50 of 11.6 μM for FL cells.

We characterize resistance phenotype of oxoglaucine with a panel of PV1pv with known resistance mutations to antivirals. Surprisingly, we found that an enviroxime-resistant mutant showed resistance to oxoglaucine treatment. This suggested that oxoglaucine is an inhibitor of PI4KB/OSBP pathway in PV replication.

In summary, we identified oxoglaucine as a PI4KB inhibitor of novel chemical structure derived from a plant. Our results indicated the existence of PI4KB inhibitors in natural products, and suggested a potential of PI4KB inhibitor for clinical use in a consecutive administration.

Grant Б-01-13/12 from the National Science Fund, Republic of Bulgaria

References:

Galabov, A. S., I. Nikolova, R.Vassileva, A.Stoyanova (2014). Antiviral combination approach: a perspective to combat enterovirus infections. - Prilozi/Contributions, 25, in press.

Arita, M., S. Philipov, A. S. Galabov (2014). Phosphatidylinositol 4-kinase III beta is the target of oxoglaucine and pachydipol (Ro 09-0179) for their anti-poliovirus activity, and locates at upstream of the target step of brefeldin A in poliovirus replication - Microbiol. Immunol., in press.

A MODERN ALTERNATIVE FOR THE PROPHYLAXIS AND TREATMENT OF INFLUENZA VIRUS INFECTION – MULTITARGET APPROACHES WITH HIGHLY EFFICIENT COMBINATIONS OF ANTIVIRAL CHEMOTHERAPEUTICS AND BIOLOGICALLY ACTIVE COMPOUNDS

Project leader: L. Simeonova, PhD

Project collaborator: Sofia University "St. Kliment Ohridski"

Research staff: E. Pavlova, PhD; L. Tancheva, PhD; G. Goujgoulova, PhD; I. Slavcheva, MS; N. Zografov, MS; G. Gegova, MS; L. Mukova, MS; K. Todorova, BS; S. Andreeva; N. Petrov, PhD

Advisors: Acad. A. S. Galabov, DM, DSc; G. Georgiev, DVM, DSc; V. Savov, DSc; M. Mileva, PhD

For the implementation of the project aims the following activities were performed:

A. (i) Antioxidant capacities of oseltamivir, ellagic acid, isprinosine were tested in model systems; (ii) Toxicity, individual and combined effects of oseltamivir with antioxidants, vitamin E and ellagic acid and the immune modulator isoprinosine in a course of prophylactic administration in mice against experimental H3N2 infection by virology methods were established; (iii) Levels of oxidative stress in experimental influenza virus infection and the effect of combination chemotherapy of specific antivirals with biological response modifiers on the reactions of oxidation and ROS formation by a standard biomarkers measurement in vitro and in vivo were measured; (iv) The effects of individual and combined courses of oseltamivir, ellagic acid and the immune modulator isoprinosine in prophylactic administration in mice against experimental H3N2 infection on drug metabolism were studied.

B. To target the main processes involved in influenza pathogenesis, we studied the effects of oseltamivir and α-tocopherol combinations against influenza A/Aichi/2/68 (H3N2) virus infection (10 MLD50) in mice. Oseltamivir was applied orally at three daily doses, 2.5 mg/kg, 1.25 mg/kg, and 0.625 mg/kg, in a 5-day course postinfection. α-Tocopherol (120 mg/kg, dissolved in vegetable oil) was administered intraperitoneally. Three schemes of α-tocopherol 5 days course were tested: onset 5 days before infection, 2 days before infection, and the day of virus inoculation. The results demonstrated a pronounced strongly dose-dependent synergistic antiviral effect of the combination α-tocopherol and 0.625 mg/kg oseltamivir when α-tocopherol was administered simultaneously with oseltamivir: a strong decrease in mortality rate (a 78% protection), and a lengthening of mean survival time by 3.2–4 days. Lung parameters showed a substantial decrease in infectious virus content (Δ logs = 3.8/4.1) and a marked diminishment of lung index

and lung pathology. Combination α-tocopherol with 1.25 mg/kg oseltamivir manifested a marked protective effect, but the effect on lung parameters was less. The combination effect of α-tocopherol with 2.5 mg/kg oseltamivir did not surpass the monotherapeutic effect of oseltamivir. When α-tocopherol was applied in courses starting 5 or 2 days before infection, its combination with oseltamivir was ineffective.

Grant B-01-19/12 of the Bulgarian Science Fund.

BALKAN ENDEMIC NEPHROPATHY

Project leaders: A. S. Galabov, MD, DSc and. M. Polenakovic, MD, DSc

Project collaborators: Department of Medical Genetics, Medical University of Sofia, Macedonian Academy of Sciences and Arts (MASA), Skopje, FYROM

Research Staff: D. Toncheva, MD, DSc and collaborators, P. Grozdanov, PhD, I. Nikolova, PhD

Bilateral joint project (2014-2015) in the frame of agreement between Bulgarian Academy of Sciences and Macedonian Academy of Sciences and Arts

BALKAN ENDEMIC NEPHROPATHY

Project leaders: A. S. Galabov, MD, DSc and V. Stefanovic, MD, PhD

Project collaborators: Department of Medical Genetics, Medical University of Sofia Serbian Academy of Sciences and Arts (SASA), Skopje, FYROM

Research staff: D. Toncheva, MD, DSc and collaborators

Internet base data for patients with Balkan endemic nephroparthy (BEN) is established, containing detailed clinical and pathological characteristics. The DNA bank on BEN patients for genomic and proteomic analyses was broaden. DNA from 22 patients was isolated. Ekzome analysis by NGS of 22 000 genes was done. Some specific and general changes in BEN associated copies were identified.

Interacademic Bilateral Collaborative Project BAS - Serbian Academy of Sciences and Arts (2014-2015)

References:

Toncheva, D., M. Mihailova-Hristova, R. Vazharova, R. Staneva, S. Karachanak, P. Dimitrov, V. Simeonov, S. Ivanov, L. Balabanski, D. Serbezov, M. Malinov, V. Stefanovic, R. Cukuranovic, M. Polenakovic, L. Jankovic-Celickovic, V. Djordjevic, Tjavtovic, D. Plaseska, A. Galabov, V. Djonov (2014). NSG nominated CELA1, HSPG2 and KCNK5 as candidate genes for predisposition to Balkan Endemic Nephropathy. Biomed. Res. International, Article ID 920723

TESTING OF VIRUCIDAL ACTIVITY IN VITRO OF GLUTARQUAT S FOR SURFACES BY THE BDS STANDARD 14476:2013: QUANTITATIVE SUSPENSION TEST (PHASE 2, STEP 1)

Project leader: L. Nikolaeva-Glomb, MD, PhD

Research staff: N. Nikolova, MS, L. Mukova, MS

It was established a reduction of the infectious virus titer by >4 lg: against poliovus 1 (LSc-2ab) by 1% Glutarquat S after 5 min treatment at both clean and dirty conditions, and by 0.5% post 10 min at clean conditions; against human adenovirus 5 (adenoid 75) by 1% Glutarquat S after 5 min treatment at clean conditions, and post 10 min at dirty conditions, and by 0.5% after 10 min at clean conditions.

Ordered by Zhivas Ltd.

THE PRIMARY LIVER CANCER IN BULGARIA: HEPATITIS VIRUSES AND ENVIRONMENTAL FACTORS

Project leaders: A. S. Galabov, MD, DSc and P. Pineau, PhD, Institut Pasteur, Paris

Research staff: L. Nikolaeva-Glomb, MD, PhD, L. Doumanova, PhD, P. Grozdanov, PhD

Research partners: R. Gaydarski, MD, DSc, Tokuda Hospital Sofia; V. Dimitrova, MD, DSc, Clinics of Surgery, Alexandrovska Hospital, Sofia

The collecting was continued of samples from patients with primary liver cancers treated surgically or undergoing the needle liver biopsy, in parallel with blood samples.

ACIP Project

INFLUENZA VIRUSES AND HOST CELL SIGNALING PATHWAYS - NOVEL TARGETS FOR ANTIVIRAL THERAPY

Beneficent: L. Simeonova, PhD

Supervisor: S. Ludwig, PhD

Host Institution: Institute of Molecular Virology, Munster, Germany

Personal grant, Project № DO 4-138/28.03.2014, BG051PO001-3.3.05-0001 „Science-Business“, Ministry Of Education And Science, Republic of Bulgaria, supported by ESF, EU

New project

SYNTHESIS AND ANTI-ENTEROVIRUS ACTIVITY OF NOVEL DIARYL ETHERS AND THEIR COMPLEXES WITH CYCLODEXTRINS

Project supervizor: L. Antonov, DSc, Institute of Organic Chemistry with Center for Cytochemistry

Project leader: A. S. Galabov, MD, DSc

Research staff: V. Dimitrov, DSc, G. Dobrikov, PhD et the team of IOCCP; I. Nikolova, PhD, A. Stoyanova, MS, L. Mukova, MS, N. Nikolova, MS, P. Grozdanov

Grant Б 02-11/12.12.2014 from the Bulgarian Science Fund

DEPARTMENT OF IMMUNOLOGY

Current projects

ANTIBODIES WITH INDUCED POLYREACTIVITY – ROLE IN IMMUNE HOMEOSTASIS AND THERAPEUTIC POTENTIAL

Project leader: Tch. Vassilev, MD, DSc

Research staff: A. Pashov, PhD, I. Djoumerska-Alexieva, PhD, M. Hadzhieva, PhD student, J. Dimitrov, Ph.D.

Polyreactive antibodies are a normal component of the immune repertoire. Interestingly, diverse redox-active substances such as ferrous ions, ROS and heme are also able to enhance polyreactivity in a fraction of IgG referred to as "induced" polyreactive IgG antibodies. The ability of IgE antibodies to acquire induced polyspecificity has not been studied so far.

The polyreactive mouse monoclonal SPE7 IgE antibody raised against dinitrophenyl (DNP) also binds unrelated proteins and aromatic compounds. We demonstrated that SPE7 interacts with heme, resulting in a substantialadditional increase in its antigen-binding polyreactivity. We compared the binding kinetics and thermodynamics of the interaction of the native and heme-bound SPE7 to DNP. These analyses revealed that despite theacquisition of numerous novel binding specificities, heme does not influence the mechanism of recognition of the cognate antigen. In addition, the acquired additional binding promiscuity did not influence the ability to elicit degranulation of SPE7-sensitized basophils. Molecular docking and fluorescence spectroscopy analyses revealed that heme binds to the variable region of IgE outside its antigen-binding sites. This finding supports the role of heme as a co-factor responsible for the observed binding polyreactivity while not affecting the interaction with its cognate antigen.

Grant DFNI-B01-29 from the Bulgarian Science Fund

References:

Hadzhieva, M., Vassilev, T.L., Roumenina, L.T., Bayry, J., Kaveri, S.V., Lacroix-Desmazes, S., Dimitrov, J.D. 2014: Mechanism and functional implications of the heme-induced binding promiscuity of IgE. Biochemistry**,** (*in pres*s).

Hadzhieva, M., Dimitrov, J., Vassilev, T. (2014). Induced polyreactivity of heme-exposed pooled human therapeutic igg (IVIG). *C. R. de l'Acad. bulgare des Sci.* (*in press*).

DESIGN OF MODIFIED IMMUNOGLOBUIN PREPARATIONS WITH ADDITIONALLY INDUCED POLYSPECIFICITY FOR PASSIVE IMMUNOTHERAPY OF SEPSIS (BULGARIAN/SWISS COLLABORATIVE PROJECT)

Project leader: Tch. Vassilev, MD, DSc

Research staff: M. Hadzhieva, PhD student, A.Pashov, PhD, I. Djoumerska-Alexieva, PhD, J.Dimitrov, Ph.D., N. Bovin, PhD, S.von Gunten, PhD

Taken together, the mechanisms of action of IVIG involve a wide spectrum of Fab-mediated and, probably, distinct Fc-mediated mechanisms, that may or may not depend on IVIG sialylation. The effects observed in various murine models may not be consistent and many of the disease-specific mechanisms must be validated in humans, as animal models only offer a limited insight into human disease and might be biased by xenogeneic or species-specific properties of IVIG. IVIG is a pluripotent drug; its complexity, together with the pathogenetic heterogeneity of autoimmune diseases, remains a challenge to the scientist and does not allow for a simplistic perspective on its modes of action.

Grant IZEBZO from the Swiss National Science Foundation

FUNCTIONAL ELIMINATION OF AUTOREACTIVE T CELLS BY ANTIBODY THERAPY IN MURINE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS AND MS

Project leader: A. Tchorbanov, PhD

Research staff: N. Mihaylova, PhD, N. Kerekov, PhD student, S. Chausheva, diploma student

Partners: J. Prechl, Ph.D., Immunology Research Group, Hungarian Academy of Sciences - Eötvös Loránd University

Systemic lupus erythematosus is a polygenic pathological syndrome with multiple organs involvement. Self-specific B cells play a main role in the lupus pathogenesis by generation of autoantibodies as well as important autoantigen-presenting cells. Autoreactive T lymphocytes, on the other hand, are responsible for B cells activation and proliferation. Therefore, both evidences promote the idea that a down-modulation of activated self-reactive T and B cells involved in the pathogenetic immune response is a reasonable approach for SLE therapy.

In our previous studies we managed to selectively suppress the anti-dsDNA specific B-lymphocytes in lupus-prone MRL/lpr mice by cross-linking B cell receptors with the inhibitory FcγRIIb receptors using a protein chimeric molecule, consisting of DNA-mimotope peptides and anti-CD32 antibody. Elimination of the dsDNA-specific B cells in experimental mice by chimera therapy prevented the appearance of IgG anti-DNA antibodies and of proteinuria.

Annexin A1 is expressed by many cell types and binds to phospholipids in a Ca^{2}+ dependent manner. Abnormal expression of annexin A1 was found on activated B and T cells in both murine and human autoimmunity suggesting its potential role as a therapeutic target. In the present study we have investigated the possibility to modulate the autoimmune response in MRL/lpr mouse model of systemic lupus erythematosus using a neutralizing anti-annexin A1 antibody. Administration of this monoclonal antibody resulted in the inhibition of T-cell activation and proliferation, suppression of

IgG anti-dsDNA antibody-secreting plasma cells, decreased disease activity and prolonged survival compared to the control group.

Grant NSF/DDVU 10-250 from the National Science Fund, Republic of Bulgaria

References:

Gesheva V., Kerekov N., Nikolova, K., Mihaylova N., Todorov T., Nikolova M., Tchorbanov A. Suppression of dsDNA-specific B Lymphocytes reduces disease symptoms in SCID model of mouse lupus. Autoimmunity 2014, 6;47(3):162-72.

SECTION OF MYCOLOGY

Current Projects:

STUDY OF THE PHYSIOLOGICAL, BIOCHEMICAL AND ECOLOGICAL CHARACTERISTICS OF MICROMYCETES RESISTANT TO HEAVY METAL STRESS

***Project leader*:** M. Angelova, DSc

Project collaborator: V. Grishko, PhD, Ukrainian Academy of Sciences, Botanical Garden

Research staff: S. Pashova, MS, R. Abrashev, PhD, E. Krumova, PhD, V. Dishliiska, MS, J. Miteva-Staleva, MS, N. Kostadinova, MS, S. Vassilev, MS, B. Spassova, MS, E. Evtova.

Soil contamination by heavy metals is consequently the most critical environmental problems as it poses significant impacts to the human health as well as the ecosystems. Abiotic stress caused by heavy metals, in inorganic and organic forms, affects the growth, morphology, and metabolism of the microorganisms in soils. While the tolerance of many filamentous fungi to a variety of heavy metals is well documented, the mechanism for this tolerance is not completely understood.The aim of the project was to investigate the relationship between oxidative stress and heavy metal exposure in resistant fungal strains and the role of antioxidant defence in this resistance.

Heavy metal resistance of 28 selected strains were performed in order to investigate their applicability as a bioremediators for polluted areas. All the fungal isolates demonstrated raised tolerance toward Cu and Zn ions compared to the isolates from unpolluted soils. The fungal strain *Aspergillus fumigatus* 3_2 isolated from a tailing pond at the copper mine "Vlajkov vruh", Bulgaria, showed a high tolerance to Cu^{2+} and Zn^{2+}. Furthermore, the the relationship between tolerance towards Cu^{2+} and Zn^{2+} and cell oxidative stress response was studied. The model strain was identified to species level by morphological and molecular methods. Fungal cultures were exposed to enhanced concentrations of metal ions. The effect of Cu^{2+} and Zn^{2+} was evaluated by the changes in fungal growth and morphology, the level of oxidative stress biomarkers, and antioxidant activities of enzymes such as superoxide dismutase (SOD) and catalase (CAT). Two different cell responses occurred: the concentrations of up to 500 μg/mL caused enhanced level of oxidative stress biomarkers (glycogen and trehalose accumulation and oxidative damaged protein content), as well as an increase in SOD and CAT activity. The treatment with concentrations from 500 to 2 000 μg/mL led to enhanced glycogen consumption, accelerated proteolysis, and decrease in SOD and CAT activity. The present results provide additional information about the participation of oxidative stress and antioxidant defense in enhanced tolerance of fungi, isolated from metal-polluted soils. Probably, survival at extremely high concentrations also requires the participation of other defense mechanism. Furthermore, enhanced understanding of all these processes will provide essential tools for efficient remediation practices.

Bilateral joint project (2013-2015) in the frame of agreement between Bulgarian Academy of Sciences and National Academy of Sciences of Ukraine.

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EFFICACY OF ANTIMICROBIAL SUBSTANCES PRODUCED BY *STREPTOMYCES* IN MODIFYING POLYMERS USED IN CONSERVATION OF PAINTINGS IN SOME ANCIENT EGYPTIAN TOMBS

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There is an undying interest to conservation and restoration of mural paintings in ancient culture heritage. Filamentous fungi play an important role in biodeterioration of these objects. This project proposes application of an effective strategy for conservation and preservation of mural paintings and other cultural heritage in Bulgaria and Egypt.

The possible effect of fungicidal compounds on 22 fungal strains isolated from acient cultural heritages was investigated. We used two microbicide - Busan® 30L and Preventol® A6, consider with requirements for the restoration practice – they should not change the appearance; must possess a broad spectrum antifungal activity; should be used in low concentrations; should not have carcinogenic effects; shoud be applyied for antifungal protection on paper, veneer, wood, leather, stone products, etc. The compounds used exhibit inhibitory activity with regard to all test mycetes. The effect was dose- and strain dependent. The minimum inhibitory concentration (MIC), fungicides and fungistatic effect of both Busan® 30L and Preventol® A6 were evaluated. These microbicides demonstrated a high supressive effect on the fungal growth and sporulation at very low concentrations. The results highlight Busan® 30L as very effective in restoration procedures, which determines its new application in the field of restoration of cultural and historical monuments.

Bilateral scientific cooperation of the Bulgarian Academy of Sciences and the Zagazig University, Egypt.

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Konstantinov, S.M., Zaharieva, M.M., Argirova, R., Najdenski, H.M. Chapter 16. Acute infectious diseases of the upper respiratory tract – classification and therapeutic approach. Acute bronchitis. In: Pharmacotherapy. Konstantinov S.M. (ed.). Publishing house Softrade Sofia, 2014, ISBN:978-954-334-166-5 (textbook in Bulgarian language)

Konstantinov, S.M., Zaharieva, M.M., Momekov, G., Najdenski H.M. Chapter 17. Pneumonia – etiology, pathogenesis, classification and antibiotic therapy. In: Pharmacotherapy. Konstantinov S.M. (ed.). Publishing house Softrade Sofia, 2014, ISBN:978-954-334-166-5 (textbook in Bulgarian language)

Ludwig-Mueller, J., Xu, J., Agostini, E., Georgiev, M. Advances in transformed root cultures for root biofactory and phytoremediation research. In: Root Engineering, Basic and Applied Concepts, series Soil Biology, vol. 40 (Morte A., Varma A., Eds.), Springer, 2014, pp. 387-405, ISBN: 978-3-642-54275-3.

Pavlova, K. Production of polymers and other compounds of industrial importance by cold-adapted yeasts. In: Cold-adapted yeast, P. Buzzini and R. Margesin (eds). Springer-Verlag Berlin Heidelberg, 2014, pp. 397-415.

Zaharieva, M.M., Konstantinov, S.M., Momekov, G., Argirova, R., Najdenski, H.M. Resistance by chemotherapy – types and mechanisms of development, classical and modern therapeuticstrategies. Chapter 7. In: Pharmacotherapy. Konstantinov S.M. (ed.). Publishing house Softrade Sofia, 2014, ISBN:978-954-334-166-5 (textbook in Bulgarian language)

Zaharieva, M.M., Najdenski, H.M. Chapter 10. Inflammation-inflammatory syndrom – causative agents, clinical features depending on the Localization site and choice of antimicrobial drugs. In: Pharmacotherapy. Konstantinov S.M. (ed.). Publishing house Softrade Sofia, 2014, ISBN:978-954-334-166-5 (textbook in Bulgarian language)

PATENTS/UTILITY MODELS

Cosmetic composition. BG Utility Model N 1856 U1 / 31.03.2014, Bulgarian Patent Office.

EDUCATION ACTIVITY

Lectures and Practical Exercise

Acad. A.S. Galabov, DSc

Course in *General Virology*, University of Forestry, Faculty of Veterinary Medicine, Sofia

Course in *General Virology*, New Bulgarian University

Corr. Member H. Najdenski, DVMS

Course in *Infectious Diseases*, University of Forestry, Faculty of Veterinary Medicine, Sofia

Practical exercises in *Infectious Diseases*, University of Forestry, Faculty of Veterinary Medicine, Sofia

Course in *Molecular Methods in Microbiology*, New Bulgarian University

Corr. Member A. Pavlov, DSc

Course in *Food Chemistry* (for BS students), University of Food Technologies, Plovdiv

Practical exercises in *Food Chemistry* (for BS students), University of Food Technologies, Plovdiv

Course in *Bioactive Substances from Cell Cultures* (for MS students), University of Food Technologies, Plovdiv

Practical exercises in *Bioactive Substances from Cell Cultures* (for MS students), University of Food Technologies, Plovdiv

Course in *Biotechnological Productions Based on Plant and Cell Cultures* (for BS students), Agricultural University, Plovdiv

Practical exercises in *Biotechnological Productions Based on Plant and Cell Cultures* (for BS students), Agricultural University, Plovdiv

Course in *Modern Technologies and Methods for Analysis of Bioactive Substances Chemistry* (for BS students), University of Food Technologies, Plovdiv

Practical exercises in *Modern Technologies and Methods for Analysis of Bioactive Substances Chemistry* (for BS students), University of Food Technologies, Plovdiv

Prof. M. Angelova, DSc

Course in *Oxidative stress* (for BS students), New Bulgarian University

Course in *Mycology* (for BS students), New Bulgarian University

Course in *Mycology* (for BS students), Plovdiv University Paisii Hilendarski.

Assoc. Prof. L. Doumanova, PhD

Course in *Immunochemistry* (for MS students), St Kliment Ohridski University of Sofia, Faculty of Chemistry

Practical exercises in *Immunochemistry* (for MS students), St Kliment Ohridski University of Sofia, Faculty of Chemistry

Assoc. Prof. L. Nikolaeva-Glomb, PhD

Course in *Bacterial and Viral Eye Infections* (for MS students), St. Kliment Ohridski University of Sofia, Faculty of Physics

Practical exercises in *Medical Virology* (for MS students), St. Kliment Ohridski University of Sofia, Faculty of Physics

Practical exercises in *General Virology*, University of Forestry, Faculty of Veterinary Medicine, Sofia

Practical exercises in *Antiviral Agents* (for MS students), St. Kliment Ohridski University of Sofia, Faculty of Biology

Assoc. Prof. S. Danova, PhD

Course in *The Probiotics* (for MS students), University of Chemical Technology and Metalurgy, Sofia, Department of Industrial Biotechnology

Assoc. Prof. S. Stoitsova, PhD

Course in *Methods of Electron Microscopy, Histochemistry and Immunocytochemistry in Cell Biology*, St. Kliment Ohridski University of Sofia, Faculty of Biology

Practical exercises in *Methods of Electron Microscopy, Histochemistry and Immunocytochemistry in Cell Biology*, St. Kliment Ohridski University of Sofia, Faculty of Biology

Assoc. Prof. Andrey Tchorbanov, PhD

Course in *Immune Response, Infections and Autoimmunity*, Ivan Rilski Hospital

Course in *Experimental Immunology,* Ivan Rilski Hospital

Course in *Animal Models for Human Diseases and Pathological Disorders,* Project for young investigators, Institute IEMPAM, BAS

Assoc. Prof. D. Beshkova, PhD

Course in *Microbial Safety of Animal Products*, (for MS students), University of Food Technologies, Plovdiv

Course in *Microbiology of Fermented Functional Foods* (for MS students), University of Food Technologies, Plovdiv

Assoc. Prof. E. Krumova, PhD

Practical exercises in *Oxidative Stress* (for BS students), New Bulgarian University

Practical exercises in Mycology (for BS students), New Bulgarian University

Assoc. Prof. Anastats Pashov, PhD

Course in *Challenges of Tumor Immunology*, Operative Program "Development of Human Resources" BG051PO001-3.3.06-0059.

Assoc. Prof. M. Mileva, PhD

Course in *Pharmacology Eye Diseases* (for MS students), St. Kliment Ohridski University of Sofia, Faculty of Physics

Practical exercises in *Pharmacology Eye Diseases* (for MS students), St. Kliment Ohridski University of Sofia, Faculty of Physic

Course in *Analytical Chemistry and Analysis of Medicinal Products,* Medical College "Yordanka Filaretova", Sofia

Practical exercises in *Analytical Chemistry and Analysis of Medicinal Product,* Medical College "Yordanka Filaretova", Sofia

Assis. Prof. M. Stoilova-Disheva, PhD

Practical exercises in *Genetics*, St Kliment Ohridski University of Sofia, Faculty of Biology

Assis. Prof. V. Nicolova, PhD
Practical exercises in *Virology*, New Bulgarian University

Assist. Prof. S. Rusinova-Videva, PhD
Practical exercise in *Mycology* (for BS students), Plovdiv University Paisii Hilendarski, Plovdiv

Assis. Prof. R.Tropcheva, PhD
Practical exercises on Secondary Metabolites Biotechnology, St Kliment Ohridski University of Sofia, Faculty of Biology

Assist. Prof. A. Marchev, PhD
Practical exercises in *Biotechnological Productions Based on Plant and Cell Cultures* (for BS students), Agricultural University, Plovdiv

Defended PhD Thesis

Gyurkovska V. JAK-STAT-dependant anti-inflammatory action of tyrphostin AG490.
Advisor: Prof. N. Ivanovska, DSc

Marchev A. Biologically active substances from rare Bulgarian Salvia species and their in vitro cultures.
Advisors: Prof. A. Pavlov, DSc.; Prof. A. Stoyanova, DSc.

Milanova V. Inflammatory and destructive potential of neutrophils in arthritic diseases.
Advisor: Assoc. Prof. P. Dimitrova, PhD

Paunova-Krasteva Ts. Phenotypic variations related with the polysaccharide antigens of *Escherichia coli* O157:H(-)
Advisor: Assoc. Prof. S. Stoitsova, PhD

Radchenkova, N. Production and characteristics of exopolysaccharide (s) synthesized by a thermophilic strain *Aeribacillus pallidus* 418
Advisor: Assoc. Prof. M. Kambourova, DSc

Slavchev G. Molecular biological and morphological aspects of L-form formation in *Mycobacterium tuberculosis* complex species
Advisor: Assoc. Prof. N. Markova, PhD

PhD students

Belenska L. *Role of complement in the processes of joint destruction in experimental models of arthritis.*
Advisor: Prof. N. Ivanovska, DSc

Ganova P. Influence of tyrosine kinase inhibitors on the processes of osteoclastogenesis in experimental arthritis.
Advisor: Prof. N. Ivanovska, DSc

Gesheva V. *Modulation of Immune response by hemocyanins from Rapana thomasiana*
Advisor: Assoc. Prof. A. Tcorbanov, PhD and Assoc. Prof. K. Idakieva, PhD

Hadjieva M.: Induced polyspecificity of antibodies.
Advisor: Prof. T. Vassilev, MD, DSc

Hubenov, V. Studies of anaerobic digestion of organic wastes at mesophilic and thermophilic conditions",
Advisors: Assoc. Prof. I. Simeonov, PhD and Assoc. Prof. D. Denchev, PhD

Ivanova I. *Antigen targeting by genetically engineered chimeric molecules*
Advisor: Assoc. Prof. A. Tcorbanov, PhD

Kerekov N. *Humanized experimental models of autoimmune and allergic diseases.*
Advisor: Assoc. Prof. A. Tcorbanov, PhD

Litova K. Microbial biodegradation of industrial pollutants of the environment
Advisor: Assoc. Prof. Z. Alexieva, PhD

Manoilov I. *Specific therapy of autoimmune diabetes in mouse and humanized models.*
Advisor: Assoc. Prof. A. Tcorbanov, PhD

Milanova V.: *Inflammatory and destructive potential of neutrophiles in arthritis.*
Advisor: Assoc. Prof. P. Dimitrova, PhD

Miteva-Staleva J. Cold stress and aging in Antarctic fungi
Advisor: Prof. M. Angelova, DSc

Pashova S. *Applied investigations of B cell populations.*
Advisor: Assoc. Prof. A. Pashov, PhD

Soykov Y. *Production and haracterization of microbial chitinases*
Advisors: Prof. A. Pavlov, DSc and Prof. A. Krastanov, DSc

Stoyanov A. Genetic and molecular studies on methylotrophic yeast *Hansenula polymorpha*
Advisor: Assoc. Prof. K. Lahtchev, PhD

Teneva Ts. *Biodiversity of lactic acid bacteria in Bulgarian medical plants and solution for using their biological potential*
Advisor: Assoc. Prof. D. Beshkova, PhD

Velikova P. Polysaccharide-modifying lactic acid bacteria with application in the food industry
Advisor: Assoc. Prof. P. Petrova, PhD

Vrancheva R. *Bioacive substanses from Bulgarian Fumaria spp*.
Advisor: Prof. A. Pavlov, DSc

Zahmanov G. *Pharmaceutically important metabolites from from Sambucus ebulus and its in vitro cultures*
Advisor: Assoc. Prof. M. Georgiev, PhD

Defended MS Diploma Thesis

Borisova D. *Comparative studies on Pseudomonas aeruginosa strains from CF patients*.
Advisor: Assoc. Prof. S. Stoitsova, PhD

Jordanova V. *Effects of novel compounds on bactyerial growth and biofilm formation*.
Advisor: Assoc. Prof. S. Stoitsova, PhD

Draganova T. *Birds as a potential vector for dissemination of bacterial pathogens in waters*
Advisor: Prof. H. Najdenski, DVM, DSc

Student practice

Bradyanova S. *Experimental immunology*
Advisor: Assoc. Prof. A. Tchorbanov, PhD

Chepinski P. *Experimental immunology*
Advisor: Assoc. Prof. A. Tchorbanov, PhD

Delcheva N. **Experimental immunology**
Advisor: Assoc. Prof. A. Tchorbanov, PhD

Dobrinov V. *Microbial degradation of phenolic compounds*
Advisor: Assoc. Prof. Z. Alexieva, PhD

Dukova M. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes*
Advisor: Assoc. Prof. P. Petrova, PhD

Giurchev N. *Biogas production*, Jacobs University, Bremen,
Advisor: Assoc. Prof. Ivan Simeonov, PhD

Gotseva I. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes.*
Advisor: Assoc. Prof. P. Petrova, PhD

Hasan Y. *Methods for determination of antioxidant activity*.
Advisor: Assist. Prof. A. Marchev

Hlebarska D. *Experimental immunology*
Advisor: Assoc. Prof. A. Tchorbanov, PhD

Jordanova V. *Practicum in microbiology*
Advisor: Assoc. Prof. S. Stotsova, PhD

Kehayova M. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes.*
Advisor: Assoc. Prof. P. Petrova, PhD

Kirilova Z. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes.*
Advisor: Assoc. Prof. P. Petrova, PhD

Kitanova V. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes*.
Advisor: Assoc. Prof. P. Petrova, PhD

Mileva K. HPLC techniques. University of Food Technologies, Plovdiv
Advisor: Assist. Prof. A. Marchev

Neycheva N. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes.*
Advisor: Assoc. Prof. P. Petrova, PhD

Pankina E. *Salvia scabiosifolia in vitro* cultures.
Advisor: Assist. Prof. A. Marchev

Papadoupolu A. *Fumaria in vitro systems*, Aristotle University of Thessaloniki, Greece
Advisor: Prof. A. Pavlov, DSc

Slavov S., *Experimental immunology*
Advisor: Assoc. Prof. A. Tchorbanov, PhD

Todorova D. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes.*
Advisor: Assoc. Prof. P. Petrova, PhD

Valdano J. *Amarallydaceae in vitro systems.* University of Alecante, Spain
Advisor: Prof. A. Pavlov, DSc

Valentinov K., *Experimental immunology*.
Advisor: Assoc. Prof. A. Tchorbanov, PhD

Yovcheva M. *Recombinant DNA technologies, applied to prokaryotes and eukaryotes.*
Advisor: Assoc. Prof. P. Petrova, PhD

CELEBRATION DAY OF THE STEPHAN ANGELOFF INSTITUTE OF MICROBIOLOGY

The Day of Institute, March 14, already turned into tradition, was celebrated with a ceremonial meeting. The meeting was opened with exciting speech delivered by the Director - Prof. H. Najdenski, Corresponding Member of BAS. Special guest and invited speaker in 2014 was Prof. Georgi Russev, Corresponding Member of BAS from Institute of Molecular Biology, Bulgarian Academy of Sciences that gave a very intriguing lecture entitled "Organisation of prokaryotic and eukaryotic genomes".

Acad. Angel S. Galabov, delivered the traditional Annual Prize for the best scientific publication by young microbiologist (under 35 year of age) to Flora Tsvetanova, PhD student (Institute of Chemistry Engineering, BAS) and Marta Encheva, PhD student (Biological Faculty, Sofia University "St. Kliment Ohridski").

ACTIVITIES OF FOUNDATION "ACAD. PROF. DR. STEPHAN ANGELOFF"

The annual awards for the best scientific publication by young microbiologist (under 35 year of age) were been given to:

Flora Tsvetanova, PhD student (Institute of Chemistry Engineering, BAS)

Tsvetanova, F., Petrova, P., Petrov, K. 2,3-Butanediol production from starch by engineered *Klebsiella pneumoniae* G31-A. *Appl. Microbiol. Biotechnol*., 2014, 98, 2441-2451

Marta Encheva, PhD student (Biological Faculty, Sofia University "St. Kliment Ohridski").

Kenarova, A., Encheva, M., Chipeva, V., Chipev, N. Hristova, P., Moncheva, P. Physiological diversity of bacterial communities from different soil locations on Livingston island, South Shetland archipelago, Antarctica. *Polar Biol*., 2014, 36(2), 223-233.

13th CONGRESS OF THE BULGARIAN MICROBIOLOGISTS WITH INTERNATIONAL PARTICIPATION

The 13th Congress of the Bulgarian Microbiologists with International Participation took place in Tryavna (Bulgaria), October 7 – 10, 2014. The Congress was organized in accordance with the By-Laws of Bulgarian Society for Microbiology at Union of Scientists in Bulgaria. The scientists of the Stephan Angeloff Institute of Microbiology (SAIM, BAS) actively participated in the organization of the Congress. Twenty five plenary lectures, 34 oral presentation as well as 48 posters revealed the latest scientific achievements in the fields of General and Applied Microbiology, Medical Microbiology, Veterinary Microbiology, Virology, Infectious Microbiology and Plant and Soil Microbiology. This forum was attended by 150 participants from 11 countries: Germany, France, Italy, Poland, Russia, Grece, Turkey, Rumunia, Serbia, Republica Macedonia, and Ukraine.

Invated speakers:

- Dietmar Fuchs, Divisions of Biological Chemistry and Medical Biochemistry, Medical University, Innsbruck, Austria

- Maria Damian, "Cantacuzino" National Institute of Research-Development for Microbiology and Immunology, Bucharest
- Milton S. Da Costa, Departamento de Ciências da Vida, Univesrsidade de Coimbra, Coimbra, Portugal
- Igor Mokrousov, Laboratory of Molecular Microbiology, St. Petersburg Pasteur Institute, St. Petersburg, Russia
- Lazar Ranin, Institute of Microbiology and Immunology, School of Medicine, University of Belgrade, Serbia
- Stoyan Grudev, University of Mining and Geology "Saint Ivan Rilski", Sofia
- Hristo Najdenski, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Sofia
- Milen Georgiev, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Sofia

MEETING OF THE INTERNATIONAL SCIENTIFIC COUNCIL OF IMicB

The first joint meeting of the International Scientific Council (ISC) of the SAIM-BAS with the members of the Scientific Counci and scientists from the Institute was held in October 6, 2014. The meeting was also attended by Prof. Elisabeth Carniel (Institute pasteur, Paris), Prof. Fabian Wild, Expert in the Centre of WHO, Lion, France, Prof. Dietmar Fuch, University of Innsbruck, Austria, Prof. Igor Mokrousov, St. Petersburg Pasteur Institute, St. Petersburg, Russia

The Director - Prof. H. Najdenski, Corresponding Member of BAS, gave a presentation highlighting the main scientific topics, fundamental and practical achievements, the existing problems, strategies and new perspectives of the scientific trends in the light of the National and European priorities. In a very constructive discussion, all present members of ISC expressed their opinions and comments, and made useful recommendations for improving the future work of SAIM-BAS.

AWARDS FOR 2014

Award of the Union of Scientists in Bulgaria – 2014

Assoc. Prof. P. Dimitrova, PhD (Department of Immunology) was awarded a price of Bulgarian Union of Scientists for 2014 year in the field of Biology and Medicine

Award of Bulagarian Academy of Sciences

Zahari Rajkov, PhD (Departament of Virology) was awarded a price of Bulagarian Academy of Sciences in a competition for high scientific achievements dedicated to the 145th anniversary of the BAS

Award of the 13th Congress of the Bulgarian Microbiologists with International Participation

Tz. Teneva, PhD student and D. Borisova, MS, were awarded a price for the best poster presented at the Conngress.

SCIENTIFIC DIVISION

DEPARTMENT OF GENERAL MICROBIOLOGY

Head of Department: Zlatka Aleksieva, PhD, Assoc. Professor

Section of Morphology of Microorganisms and Electron Microscopy

Head: Stoyanka Stoitsova, PhD, Assoc. Professor
Tsvetelina Paunova, MS, Assist. Professor
Ivan Chavdarov, MS, Electronic Engineer
Nina Tadjer, BS, Laboratory Assistant
Lidana Panova, BS, Laboratory Assistant
Dajana Borisova, Microbiologist

Section of Microbial Genetics

Head: Zlatka Aleksieva, PhD, Assoc. Professor
Kantcho Lahtchev, PhD, Assoc. Professor
Svetla Danova, PhD, Assoc. Professor
Penka Petrova, PhD, Assoc. Professor
Maria Gerginova, PhD, Assist. Professor
Margarita Stoilova, PhD, Assist. Professor
Nadejda Peneva, MS, Assist. Professor
Jordan Manasiev, PhD, Assist. Professor
Dimitrinka Lyutskanova, PhD, Assist. Professor
Galina Stoyancheva, PhD, Assist. Professor
Dillnora Gouliamova, PhD, Researcher
Vesela Peltekova, Technician
Rositza Tropcheva, PhD student
Anton Stojanov, PhD student

Section of Microbial Biochemistry

Head: Tatyana Avramova, PhD, Assoc. Professor
Blaga Angelova, PhD, Assoc. Professor
Evgenia Vasileva-Tonkova, PhD, Assoc. Professor
Nelly Christova, PhD, Assist. Professor
Anna Sotirova, MS, Assist. Professor
Stephan Engibarov, MS, Assist. Professor
Rumyana Eneva, MS, Assist. Professor
Irina Lazarkevich, MS, Assist. Professor

DEPARTMENT OF APPLIED MICROBIOLOGY

Head of Department: Atanas Pavlov, DSc, Professor

Laboratory of Microbial Biosynthesis and Ecology

Head: Kolishka Tcekova, PhD, Assoc. Professor
Adriana Gousterova, PhD, Assoc. Professor
Lyudmila Kabaivanova, PhD, Assoc. Professor
Aleksaner Hristov, PhD, Assist. Professor
Aleksander Krumov, PhD, Assist. Professor
Dessislava Todorova, PhD, Assist. Professor
Ignat Dimov, Assist. Professor
Lilyana Nacheva, Assist. Professor
Krasya Aleksieva, Researcher
Donka Paskaleva, Researcher
Philip Philipov, Researcher
Rositca Petkova, Researcher
Anna Brachkova, PhD student

Laboratory of Extremophilic Bacteria

Head: Margarita Kambourova, DSc, Assoc. Professor
Ivanka Bojadzhieva, PhD, Assist. Professor
Miroslava Atanasova PhD, Assist. Professor
Iva Tomova, PhD, Assist. Professor
Nadja Kirilova, MS, Assist. Professor
Nikolina Atanasova, MS, Researcher

Laboratory of Applied Biotechnologies

Head: Atanas Pavlov, DSc, Professor
Milen Georgiev, PhD, Assoc. Professor
Kostanca Pavlova, PhD, Assoc. Professor
Dora Beshkova, PhD, Assoc. Professor

Ginka Frengova, PhD, Assoc. Professor
Vasil Georgiev, PhD, Assist. Professor
Snejana Videva, PhD, Assist. Professor
Katerina Georgieva, MS, Microbiologist
Tatyana Gocheva, Technologist
Elka Genova, Technologist
Svetla Stojkova, Technologist
Vasilka Ushterova, Laboratory Assistant
Andrei Marchev, PhD student
Tzvetanka Teneva, PhD student
Yuri Stoikov, PhD student
Georgi Zahmanov, PhD student

Research group of Mathematical modelling and Computer Methods
Head: Ivan Simeonov, PhD, Assoc. Professor

Elena Chorukova, PhD, Assist. Professor
Venelin Hubenov, Assist. Professor
Snezhanka Mihaylova, MS, Technologist
Georgi Valevski, Dipl. eng.

DEPARTMENT OF INFECTIOUS MICROBIOLOGY

Head of Department: Hristo Najdenski, DVM, DSc, Professor

Laboratory of Zoonozes and Bacterial Virulence

Head: Hristo Najdenski, DVM, DSc, Professor
Maya Zaharieva, PhD, Assist. Professor
Tanya Dimova, PhD, Assist. Professor
Zvezdimira Tcvetanova, PhD, Assist. Professor
Trayana Draganova, MS, Researcher
Dimitar Dimitrov, Assist. Professor
Vanja Slaveva, Researcher
Maya Gatzovska, MS

Laboratory of Genetics and Resistance of Mycobacteria

Head: Nadya Markova, MD, PhD, Assoc. Professor
Violeta Valcheva, PhD, Assist. Professor
Georgi Slavchev, MS, PhD student
Albena Cherneva, Researcher

Laboratory of Antimicrobial Agents

Head: Vesselin Kussovski, PhD, Assoc. Professor
Iva Tzvetkova, MS, Researcher
Mariana Ninova, MS, Assist. Professor
Tchavdar Tankov, Laboratory Assistent

DEPARTMENT OF VIROLOGY

Head of Department: Lyubomira Nikolaeva, MD, PhD, Assoc. Professor

Academician Angel S. Galabov, MD, DSc, Professor

Laboratory of Viral Proteins

Head: Lyubka Doumanova, PhD, Assoc. Professor
Milka Mileva, PhD, Assoc. Professor
Yurii Abashev, PhD, Assist. Professor
Adriana Dimitrova, PhD student

Laboratory of Experimental Chemotherapy of Enteroviral Infections

Head: Ivanka Nikolova, PhD, Assist. Professor
Lyubomira Nikolaeva, MD, PhD, Assoc. Professor
Nadya Nikolova, MS, Researcher

Laboratory of Experimental Chemotherapy of Influenza

Head: Lora Simeonova, PhD, Assist. Professor
Galina Gegova, MS, Researcher
Kirilka Todorova, BS, Technician
Snejana Andreeva, Laboratory Assistant

Laboratory of Oncolytic Viruses

Head: Assya Angelova, PhD, Assist. Professor
Zahari Raykov, MD, PhD, Assist. Professor
Neli Vilhelmova, PhD, Assist. Professor
Adelina Stoyanova, MS, Assist. Professor
Luchia Mukova, MS, Researcher

DEPARTMENT OF IMMUNOLOGY

Head of Department: Nina Ivanovska, DSc, Professor

Laboratory of Experimental Immunotherapy

Head: Anastas Pashov, PhD, Assoc. Professor
Tchavdar Vassilev, MD, DSc, Professor
Iglika Djoumerska-Alexieva, MD, PhD, Assist. Professor
Maya Hadjieva, PhD student

Laboratory of Experimental Immunology

Head: Andrey Tchorbanov, PhD, Assoc. Professor
Nikolina Mihaylova, PhD, Assist. Professor
Kalina Nikolova-Ganeva, PhD, Assist. Professor
Ilian Manoilov, PhD student
Nikola Kerekov, PhD student
Viktoriya Milanova, PhD student

Laboratory of Infectious Immunology and Inflammation

Head: Nina Ivanovska, DSc, Professor
Petya Dimitrova, PhD, Assoc. Professor
Tsvetanka Stefanova, PhD, Assist. Professor
Petya Stoyanova, DVM, Researcher
Iva Ivanova, PhD student
Petya Ganova, PhD student
Valeriya Gyurkovska, PhD student

SECTION OF MYCOLOGY

Head: Ekaterina Krumova, PhD, Assoc. Professor
Radoslav Abrashev, PhD, Assist. Professor
Nedelina Kostadinova, PhD, Assist. Professor
Svetlana Pashova, MS, Assist. Professor
Vladislava Dishliiska, MS, Assist. Professor
Jeni Miteva-Staleva, MS, Assist. Professor
Borjana Spasova, MS, Researcher
Emilia Eftova, Laboratory Assistant

LABORATORY CENTER PASTEUR

Head: Peter Grozdanov, PhD, Assist. Professor
Anna Terziyska, PhD, Assist. Professor
Ina Ivanova, MS

ADMINISTRATIVE AND TECHNICAL DIVISION

Secretariat
Petya Nikolova, Coordinator
Nadka Panova, Human Resources
Ivailo Georgiev, MS, IT Servicep eng
Krasya Nenova, Technical secretary
Ivan Georgiev, Secretary
Nora Toupareeva, Courrier

Accountancy
Antoaneta Tcareva, Chief accountant
Stefka Yonkova, Accountant
Snezhanka Daskalova, Accountant-cachier
Violeta Manolova, Accountant

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Lora Simeonova, PhD, Assist. Professor

Library
Todorka Kehajova, Librarian
Anna Vaneva, Researcher

BIOLOGICAL SERVICES

Laboratory Cultural Media
Nataliya Georgieva, MS, Researcher
Dima Kuzarova, MS
Krasimira Beshkova, Technician

Fermentation Laboratory
Spasen Vassilev, Assist. Professor
Vesselina Pankova, MS, Researcher eng.
Galina Nikolova, MS

Animal House Facility
Petya Stoyanova, DVM, Researcher
Eleni Axioti Dimitrova

Technical Service
Evgenia Minkova, Asssitant director, eng.

Electro-Mechanical Workshops
Dimiter Brajnov
Plamen Stefkov
Tzvetanka Begova

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Hristo Najdenski	Professor, DSc, Corresponding member of BAS
Atanas Pavlov	Professor, DSc, Corresponding Member of BAS
Todor Kantardjiev	Professor, DSc
Maria Angelova	Professor, DSc
Nina Ivanovska	Professor, DSc
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